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Radioterapia di precisione per un'oncologia innovativa e sostenibile

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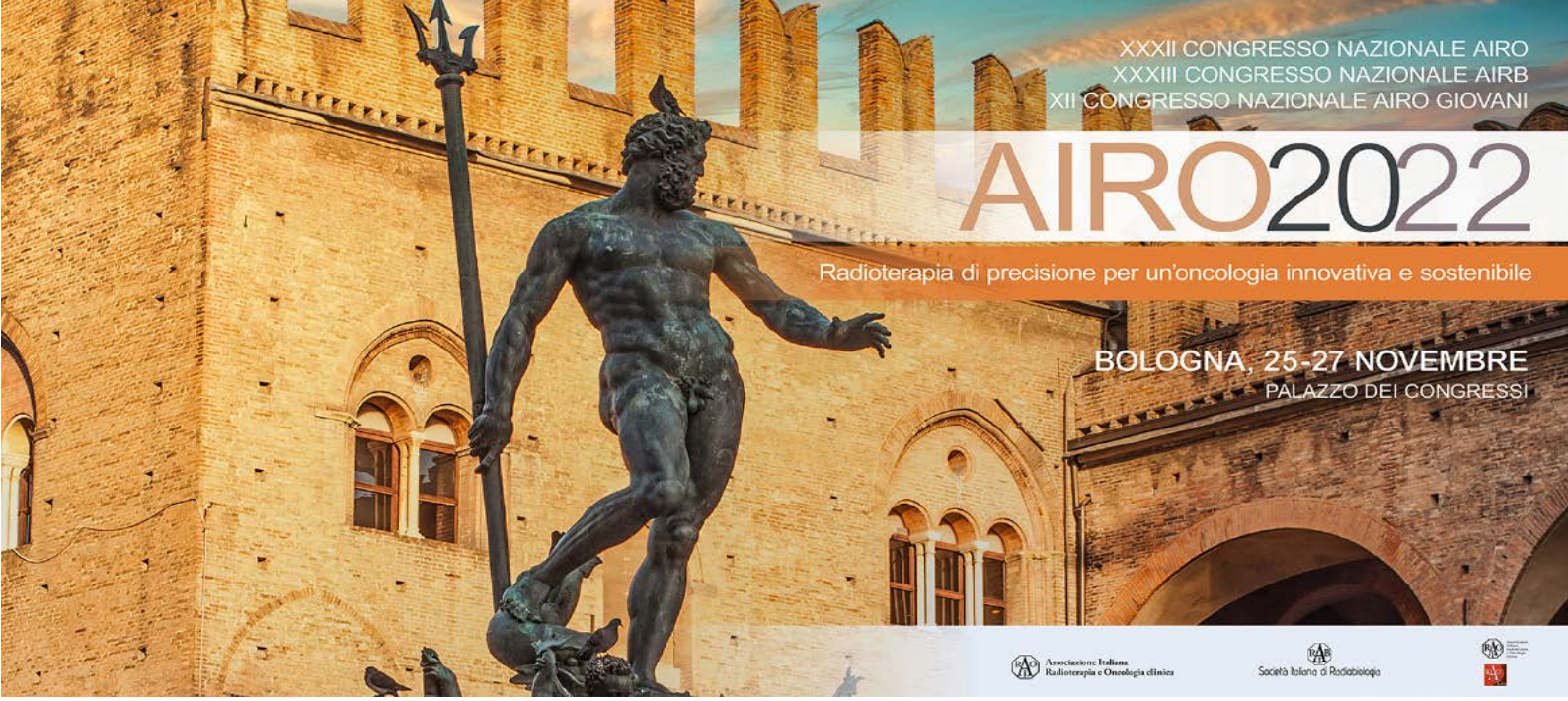

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Programme

STEREOTACTIC RADIOTHERAPY: STANDARD AND INNOVATION IN THE CLINICAL PRACTICE

L. Nicosia

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Stereotactic Radiotherapy is the standard for the treatment of several primary and secondary malignancies. Apart from well-established indications like lung and prostate cancer or brain metastases, new promising evidence is supporting its use also in new or relatively new fields. Also tecnological innovations permit today the delivery of safe and accurate treatment in an efficient way.

In the first part of this presentation it will be discussed the current clinical standard of treatment in the field of prostate adenocarcinoma, brain metastases, pancreatic tumor, abdominal metastases. The last clinical trial supporting their use will be discussed as well. The topic of the second part will be the role of new technologies that might improve the current clinical practice. A particular focus will be on MR-linacs for the treatment of prostate cancer, pancreatic carcinoma, liver and lymphnode metastases. Another section will be dedicated to the current modern approach to brain metastases using linac-based monoisocentric technique. In the last part of the presentation the emerging role of radiomics and artificial intelligence and their actual clinical applications.

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"BACK TO THE N.O.RT (NOT-ONCOLOGICAL RADIOTHERAPY)": USE OF RADIOTHERAPY FOR NOT-ONCOLOGICAL DISORDERS

F. Gagliardi, V. Nardone, A. Sangiovanni,
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Radiation therapy (RT) is an effective cancer treatment. In the last decades, RT has undergone several advances due to the increase in knowledge of radiobiology, use of advanced imaging and treatment delivery approaches. The introduction of novel systemic therapies and the use of altered fractionation schedules, could lead to a decrease in the percent of patients receiving radiotherapy for cancer disorders in the next future.[3]

Therefore, it becomes necessary for radiotherapist to tend to look toward other branches of medicine.

This scenario is already real in Germany, where not oncologic RT (NORT) disease represent the 20% of patients treated with RT. Furthermore, since 1995 there is a specific task force, the German Cooperative Group on Radiotherapy for Benign Diseases (GCG-BD), that revised the past clinical experience to define National guideline of NORT.[1]

In Italy, NORT is poorly used, because the low interest of radiotherapist in not oncology patients and the poor experience of the other specialists that are not aware of the possibility of using RT for their specialty.

In the past, NORT had been used in benign condition but with poor results due to an unreliable dosimetric study and adverse events as high risk of secondary cancers like leukemia.[2]

Nowadays, through the experience in the oncological field and the accurate technological advance, NORT could be used in in different medical branches with low risk of chronic adverse event (Table 1).

Finally, seen the optimistic results of these studies, the NORT can be considered safe and effective for the not malignant disease, and it would be interesting if also in Italy we could create a specific task force for the widespread of the NORT for the consolidated pathologies and future research prospective.

Considering the increased life expectancy and the higher number of older patients ineligible for invasive treatment, the use RT could be important for the prevention or reduction of pain and the improvement physical body functions of patients with not malignant diseases.

In conclusion, the use of the NORT needs to be promoted in order to open up new avenues for our discipline and allow us to expand into the great world of medicine outside the oncology area.

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Table 1.

NCT Number	Disease	Design	Location
NCT04722263	Keloids	Single arm, interventional pilot study (15 patients). RT: 15 Gy in 3 fractions.	Montefiore Medical Center, New York, US
NCT04122313	Dupuytren's Disease	Prospective, Cohort study. Participants will be treated according to a standard treatment pathway, followed by post-operative radiation. RT: 15 Gy in 5 fx, followed by a 6-8 weeks break then a second identical course. Total dose: 30Gy.	University of Minnesota, US
NCT04424628	Gonarthrosis and Coxarthrosis	Non-inferiority study in which the investigators compare two low-dose radiotherapy schemes. Arm A will be treated at 3 Gy (0.5 Gy/fraction, 3 fractions/week), and patients in arm B will be treated at 6 Gy (1 Gy/fraction, 3 fractions/week).	GenesisCare, Malaga, Spain
NCT02708810	Trigeminal Neuralgia	To determine the feasibility of frameless Virtual Cone trigeminal neuralgia radiosurgery at a single institution prior to multi-institutional enrollment.	Hazelrig-Salter Radiation Oncology Center, Birmingham, Alabama, US
NCT03995823	Cerebral Arteriovenous Malformations	Prospective study including 50 patients with cerebral AVMs treated with GRKS to evaluate the sensitivity for nidus obliteration of MRI.	Department of Neurosurgery, Medical University of Vienna, Austria
NCT04843683	Cardiac Arrhythmias	Prospective, single-center, phase II trial that will be monitoring the safety and efficacy of using stereotactic ablative radiotherapy (SBRT) to treat arrhythmias.	University Health Network, Toronto, Canada
NCT04984265	Cardiac Arrhythmias (Chagas)	SBRT in Chagas Disease Ventricular Tachycardia. A single 25Gy dose will be delivered to the PTV.	University of Sao Paulo General Hospital, Sao Paulo, Brazil

COME LA PANDEMIA HA CAMBIATO LA PRATICA CLINICA: DALLA TELEMEDICINA AGLI IPOFRAZIONAMENTI

F. Gregucci[1], R. Carbonara[1], A. Ciabattoni[2], M. Caliandro[1], A. Surgo[1], M.P. Ciliberti[1], E. Paulicelli[1], I. Bonaparte[1], A. Fiorentino[1]

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Worldwide, the COVID-19 pandemic has had a significant impact on cancer care due to the conditions linked to the emergency.[1] In this situation, a reorganization of health resources was mandatory, on the one hand to avoid excessive exposure to infectious risk, and on the other to avoid that life-saving treatments could not be carried out correctly.[2] The Radiation Therapy (RT) has found its place with the need to prioritize essential treatment.[3] Several papers have been published regarding the RT management of cancer patients during COVID era.[4,5] Based on this background, aim of this review is to synthesize the emerging changes in multiple fields of Radiation Oncology, reporting an overview of high-quality clinical experiences and recommendations published.

Methods: The literature review was performed according to a Pubmed/MEDLINE search via P (population) I (intervention) C (comparison) O (outcome). The search keywords were "Covid AND Radiotherapy", "Covid AND Hypofractionated Radiotherapy" and "Covid AND Telemedicine". Only higher quality articles in English language were included.

Results: Overall, an exponential growth of publications regarding COVID-19 and RT was observed over time.[6] The recommendations and consensus proposals of international experts for the management of cancer patients during the COVID-19 pandemic have been published regarding almost all oncological diseases. The remarked endpoint of published works was the balance between the risk of oncological disease progression and ill from COVID-19. In general, the use of RADS (Remote, Avoid, Defer, Shorten) principles has been proposed, taking into account the necessity of personalized therapeutic approaches, which can be summarized in the following points:

- consider the possibility of treating COVID-positive patients in selected cases;
- prioritize treatments based on the biological aggressiveness of the cancer and treatment purpose;
- preferably use hypofractionated schedules and highly favor stereotactic RT treatments when clinically indicated.

The evaluation of patient-specific risk factors and a multidisciplinary management remain crucial steps of diagnostic-therapeutic care pathways.

Conclusions: In conclusion, during COVID-19 pandemic, the health system organization should be completely restructured, switching "from Evidence-Based Medicine (EBM) to Emergency-Based Medicine (EMBM)", optimizing the resources.

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ONCOLOGICAL PREVENTION AND "INTERCEPTION": TOWARDS PERSONALIZED MEDICINE

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While preventive efforts have made great strides in reducing mortality from diabetes and cardiovascular pathologies, cancer is often diagnosed at advanced stages. Early detection is still challenging for many malignancies.

Targeted and immune therapies have emerged as powerful weapons. Still, for a large number of neoplasms – including pancreas, liver, lung, esophagus, brain, stomach, and ovary – survival at five years is still less than 50%, especially when patients present with late-stage disease. Progress in preventing cancer is urgent, due to increases in the population, longer life spans and higher risk.

Improving preventive measures for one disease can also protect against the onset or severity of another, as was shown during the COVID-19 pandemic, where hypertension, obesity, type 2 diabetes, ischemic heart disease, and heart failure influenced disease outcome.

Many cancers (over 30%) can be prevented by lifestyle, by avoiding risk factors such as tobacco use, excessive UV exposure, infectious agents, as well as poor dietary habits, lack of exercise, overweight, and obesity. Genetic counseling in case of genetic predisposition and screening programs can help hindering or detecting certain types of cancer before signs or symptoms appear.

Molecular techniques and "big data" are opening up new avenues for efforts aimed at decreasing cancer incidence and death. We are moving toward precision prevention, better tools for early detection and for risk assessment, the use of a Precancer Atlas, unveiling of new biomarkers. Besides improving lifestyle, many other factors can impact cancer risk: gender, ethnicity, geographical and economic differences are associated with disparities in prevention, which we want to overcome. There is a warning to consider a multifaceted molecular but also social approach.

In this complex scenario, stopping cancer before it starts or, in the second instance, before it becomes fatal, in a prevention or interception setting, remains a challenging task.

THE ECONOMIC SUSTAINABILITY OF INNOVATIVE RADIOTHERAPY

M. Barbieri

York Health Economic Consortium

The rapid diffusion of new technologies has been proposed as a major cause of increasing healthcare costs. Radiation oncology, a high-tech discipline in continuous evolution through a combination of new treatment schedules, more advanced techniques and novel technologies, does not remain spared of these increasing financial demands. It is well-known that insufficient financing delays the implementation of health innovations. Health technology assessment (HTA) and economic evaluation can help decision makers to invest on technologies that guarantee good value for money. HTA builds on clinical evidence and encompasses a comprehensive multidisciplinary process that evaluates the social, economic, organizational and ethical issues related to a health intervention or technology. The decision on which new healthcare interventions to adopt in routine practice inherently needs to rely on a trade-off between the costs and the expected benefits. This is classically performed through economic evaluations, where the extra cost of a new intervention (compared to the standard treatment) is balanced to the additional gain in clinical effect. Although economic evidence has become mandatory to support healthcare decision-making regarding new therapeutic interventions, challenges remain in generating high-quality cost and cost-effectiveness data. This is especially the case for complex and rapidly evolving treatment modalities such as radiotherapy, where therapeutic benefits may only become apparent after many years. Also, new radiotherapy approaches tend to be more costly during the implementation and learning phase. These uncertainties inherently related to the gradual process of radiotherapy evolution, influencing outcome as well as costs, make cost-effectiveness analyses more difficult to accomplish. If we want to tap the full potential of promising innovations and assure that our patients get access to high-quality radiotherapy, while avoiding unacceptable impact on the healthcare budgets under pressure, we have to accept new means of developing clinical and economic evidence. Methods of cost-effectiveness analyses will be illustrated by means of examples for new radiotherapy techniques.

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HADRONTHERAPY: GENERAL CONCEPTS AND MAIN INDICATIONS

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Hadrontherapy involves the use of proton and carbon ions. Due to its physical characteristics particle therapy exhibits a Bragg peak, concentrating dose within tumor and minimizing damage to surrounding structures, with evidence of toxicity reduction versus photon.[1] The most common particle therapy is proton, with a relative biological effect (RBE) roughly 1.1 times that of photon,[2] with recent data suggesting an RBE up to 1.3 that is both cell line and fraction size dependent in H&N cell lines.[3] Proton therapy (PT) is particularly useful in tumors in proximity to numerous critical structures. Due to a variable RBE approximately about 3, carbon ion radiotherapy (CIRT) is suitable for rare, radioresistant and recurrent tumors. It is characterized by high LET, low cell cycle dependence an effect on the hypoxic tumors.[4] According to essential levels of assistance particle therapy may be indicated for several histologies such as chordoma and chondrosarcomas of the base of the skull and spine, head and neck, paraspinal, retroperitoneal and pelvic sarcomas, osteosarcoma, chondrosarcoma, intracranial meningiomas in critical locations (close proximity to the optic pathways and the brainstem), orbital and periorbital tumors, ocular melanoma, adenoid- cystic carcinoma of the salivary glands, solid pediatric tumors, tumors in patients with genetic syndromes and collagen diseases, previously re-irradiated relapses. Rates of local control and progression free survival in those tumors treated with PT or CIRT are promising, as established by recent studies.[5-8] Apart from these indications, it is still a challenge to establish which patient would benefit the most from particle therapy. Recent literature describes strategies to compare protons and photons, exploring the role of an approach to select patients for particle therapy.[9] Due to

the limited access to PT facilities and higher costs, in the Netherlands Langendijk *et al.*[10] developed the so-called Model-based approach (MBA). It is based on the principle that the risk of radiation-induced side effects can be predicted by multivariable normal tissue complication probability models. In the near future when PT centers will be increasingly common, it will be essential to establish which tumor and which patient would benefit most from particle therapy. Alternative methods to randomized clinical trials such as the MBA could find a role in the selection of patients.

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TREATMENT OF STAGE IV NON-SMALL CELL LUNG CANCER

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Algorithms in the treatment of advanced non-small cell lung cancer (NSCLC) continue to evolve as new therapeutics show positive efficacy improvements. The development of new molecular therapies targeting particular abnormalities such as mutations in the EGFR (Epidermal Growth Factor Receptor) gene or ROS1 or ALK genes rearrangements resolved in novel strategies in advanced NSCLC management. Immunotherapy, with or without chemotherapy, is now the standard of care in the first-line setting in patients without EGFR, ALK, or ROS driver mutations.

For the oligometastatic setting, radiotherapy to both primary and metastatic lesions might prolong both progression-free survival and overall survival. The combination of targeted treatments and radiation is an encouraging and promising strategy for advanced oncogene driver-mutated NSCLC. The concept of targeting oligoprogressive disease while continuing systemic therapy beyond progression is increasingly performed. There is emerging evidence that radiotherapy not only provides local tumour control but also may influence systemic control, when combined with immunotherapy.

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RADIOBIOLOGIA ED IPOFRAZIONAMENTO

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Due to technological advances in the past 2 decades allowing high conformality and steep dose gradients, hypofractionation have become the dominant prescription

regimen as compared to its relative modest and often "palliative" use in the late twentieth century. However the biology of hypofractionation is still perceived as contradictory and confusing. It could be proposed that the basic principle of "conventional" radiobiology in the form of the five R's of radiobiology may still apply, although hypofractionation (particularly extreme hypofractionation as seen in SBRT) due to larger dose per fraction and reduced treatment time might alter some important aspects of response to radiation or trigger non-canonical biological pathways. These considerations may even question the use of the Linear Quadratic model for the calculation of isoeffects. The radiobiological specificities of hypofractionation should be considered from preclinical research to clinical trial design.

PRECISION RADIATION THERAPY IN INNOVATIVE, SUSTAINABLE ONCOLOGY "LYMPH NODE IRRADIATION IN BREAST CANCER: WHEN AND WHAT?"

C. Aristei

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As breast cancer is a heterogeneous group of diseases with distinct molecular aberrations, the benefits of postoperative radiation therapy (RT) vary in diverse subgroups.[1] Tailoring therapy, *i.e.* treatment de-escalation for low-risk patients and escalation for high-risk cases, leads to precision medicine which aims at identifying the best approach for each individual but gives rise to several areas of contention.

Although indications for regional node irradiation (RNI) are well defined in patients with T1-2 disease and 4 or more involved axillary nodes or T3-4 disease any N, doubts persist as to whether the internal mammary nodes need to be irradiated.[2-4] Also under debate is the approache to follow after mastectomy in pT3N0 patients.

In early-stage breast cancer patients with 1-2 positive sentinel node/s (SLN) who had not received axillary lymph node dissection (ALND), randomized controlled studies showed the non-inferiority of a conservative approach (no ALND vs ALND);[5-7] areas of discussion are RT indications and volumes in candidates for irradiation.

The last hot topic in regional treatment of breast cancer is the RT approach when 1. the axilla is clinically positive and SLN/s is/are negative after neoadjuvant systemic therapy (NST); 2. the axilla is clinically negative but SLN/s is/are positive after NST.[8] In its breast cancer multidisciplinary meetings each radiation oncology centre has to engage in decision-making discussions on how to manage these patients while still awaiting the results of randomized clinical trials that were specifically designed to provide answers to these questions.

The moderate hypo-fractionated schedule (40 Gy in 15 fractions) is standard of care for RNI. The FAST Forward trial's interim analysis at 2-3 years' follow-up suggested there were no differences in arm or shoulder adverse effects after 26 Gy in 5 fractions or 40 Gy in 15 fractions; definitive assessment of non-inferiority will, however, be available only at the 5-year analysis.[9]

Finally, it is worth noting that indications for RNI in breast cancer patients need to be analyzed in light of tumour bio-pathological subtypes and genetics, modern imaging modalities, the role of systemic therapies in loco-regional control and an individual radiosensivity assessment.

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THORACIC RADIOTHERAPY AND PROPHYLACTIC CRANIAL IRRADIATION IN LS- SCLC: WHICH NEWS IN CLINICAL PRACTICE?

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A brief overview on current radiotherapy standards for both thoracic and cranial irradiation of limited stage

small cell lung cancer (LS-SCLC) will be presented. Radiotherapy is the cornerstone treatment modality in the management of (LS-SCLC), jointly with platinum-based chemotherapy. Although LS-SCLC is potentially curable with definitive chemoradiation, outcomes remain poor. In the "very limited disease" (T1-T2/N0) resection should be considered, while as stereotactic radiotherapy can be an alternative in patients not suitable for surgery. Conversely, concomitant or sequential radio-chemotherapy is the gold standard for those with node-positive disease; for whom a bifractionated schedule should be preferred up to 45 Gy. Early start of radiotherapy is strongly recommended. Limited data are available for hypofractionated treatment in this clinical setting. In the "once daily" radical treatment doses up to 70 Gy have been used in many trials; and contouring guidelines have recently been published. Prophylactic brain radiotherapy is strongly advised in patients with stage II or III, and younger than 70 years, who responded to radiochemotherapy; in patients in I stage and older than 70 years, follow up with brain magnetic resonance imaging (MRI) is the preferred option. The use of hippocampal avoidance is under investigation. Integration with immunotherapy is now extensively studied, as well as predictive and prognostic biomarkers, which are definitively needed to further improve the therapeutic index of local approaches.

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WHICH ROLE OF RADIOTHERAPY IN EXTEDENDED DISEASE SCLC IN THE ERA OF NEW SISTEMIC THERAPIES?

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Extended disease small cell lung cancer (ED-SCLC) is a poor prognosis disease; standard treatment of ED-SCLC has been represented for decades by chemotherapy with a platinum compound and etoposide. Recent studies have shown that the addiction of immunotherapy to chemotherapy has a significative advantage. Durvalumab has been tested in Caspian trial and atezolizumab in IMpower 133 trial.

Thoracic radiotherapy and profilactic cranial irradiation (PCI) in ED-SCLC have been tested in several studies conducted in the pre-immunotherapy era.

In thoracic radiotherapy there are debates concerning doses, volumes, optimal candidates to local treatments and timing in relation with sistemic treatments.

Concerning PCI some series demonstrated an advantage in terms of intracranial disease control, not always followed by an advantage in overall survival.

Impower 133 and Caspian are trials which have been developed in a medical oncology prospective and did not evaluate the role of thoracic radiotherapy, so that it represent an unmet need at the moment. In the same time, IMpower 133 and Caspian allowed PCI in accordance with clinical routine practice.

The role of PCI and the optimal integration with chemo-immunotherapy is still debated.

INTEGRATION WITH IMMUNOTHERAPY/CHEMOTHERAPY

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Reirradiation has long remained an unpopular treatment option due to fear of excessive toxicity, unpredictable dose delivery beyond the normal tissue tolerance and limited reliable imaging modalities. However, recent advances in dose delivery, intensity modulation, plans overlay, and image guidance have allowed re-irradiation to be considered as a feasible treatment option for recurrent tumors. In this reirradiation setting, increasing efforts have been made in enhancing both radiation sensitivity and efficacy by combining chemotherapy and immunotherapy with radiotherapy. Considering that after first line treatments tissues and organs show impaired function and reserve capacity, strategies that could increase the tumor cell kill of reirradiation without increasing serious toxicities would improve the therapeutic index. Many studies on reirradiation of different tumor types have reported on[1-4] multimodal approaches com-

bining radiation and various drugs. However, unlike first-line radiation regimens that have been tested in several large prospective randomized trials, reirradiation studies suffer from lack of homogeneity and much smaller numbers to draw statistically sound conclusions. Hence, the current practice is extrapolated from first-line experience and the impact of the combined approach is still not clear, regardless of the endpoint considered. At the same time, the underlying cellular and molecular mechanisms of reirradiation in combination with chemotherapeutic drugs are still far from being elucidated. Notwithstanding, the number of studies evaluating the potential of combined treatments in the reirradiation setting is increasing slowly. Proper study design, patient selection, timing and combination of treatments, and impact of fractionation schedules should be envisaged as the key points to be addressed in future trials to shed new light on the synergistic integration between reirradiation and immune/chemotherapy.

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INTEGRATION WITH TARGETED THERAPY

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Reirradiation is today still considered as a clinical challenge, due to a high incidence of toxicity, especially in in-field recurrence within a short period of time. The improvement of modern radiotherapy (RT) tecquiniques such as intensity modulated (IMRT), stereotactic body radiotherapies (SBRT) and Particle Therapy (PT), has led to improved tumor control with less severe toxicity with encouraging outcomes. The advances in precision RT match to the efforts in precision cancer medicine that are leading to increasingly personalized treatments. The advent of Immunotherapy and Targeted Therapies have improved patient outcomes particularly in locally advanced, recurrent or metastatic disease.[1]

Cancer cells have a several genetic or microenvironmental biological factors that cause progression and radioresistance. For example, KEAP1 and NFE2L2 mutations have been identified as markers of radiation resistance in lung squamous cell carcinomas. In hepatocellular carcinoma, mutations in KRAS and TP53 have been significantly associated with risk of local failure after proton therapy. Similarly, in rectal adenocarcinoma, concurrent KRAS and TP53 mutations have been associated with an insufficient response to neoadjuvant chemoradiotherapy.[2]

Several data, showed that RT has both immunostimulatory and immunosuppressive property, including changes in tumour microenvironment, altered cytokine expression, upregulation of transcription factors, induction of cell death, and promotion of antigen cross-presentation. Positive effect of radiation often predominate over negative ones but are insufficient to shift the balance of the immunosuppressive tumor microenvironment to achieve tumor response.[3] Molecular targeted drugs can be of use to overcome these inherent process and sensitise tumour cells to radiotherapy.

Preclinical models had already tested the advantages of the interaction between targeted agents and radiotherapy but this combination not always translated into an overall survival advantage for patients with cancer. Despite the promising rationale, the combination is an area of ongoing research, especially to identify potential increasing of side-effects of these approaches.[4]

Many studies are nowadays ongoing to investigate the safety, feasibility and outcomes of reirradiation in combination with targeted therapy in recurrent/metastatic cancer [NCT00970502; NCT05526924; NCT00713219].

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EARLY-ONSET PROSTATE CANCER: SURGERY, RADIOTHERAPY AND STRATEGIES FOR DOSE INTENSIFICATION

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Prostate cancer (PCa) represents the most common tumour in men and it is responsible for nearly 375.000

deaths per year worldwide.[1] Despite its usual indolent clinical course at disease onset, PCa still remains a major health burden with mortality rates expected to grow in the coming decades. Although the highest incidence of this tumor is observed in patients older than 65, more than 10% of cases occur in men aged 55 and younger.[2]

The influence of age at diagnosis on prostate cancer outcomes is unclear; according to some studies, early onset PCa may harbour mutations responsible for a more aggressive disease[3] and at least a subgroup of younger patients may have an overall poorer prognosis than older patients, after adjustment for clinical prognostic factors.

Based on these results, recently proposed STAR-CAP staging system indicates young age (<50 years) as a negative prognostic factor for Prostate Cancer Specific Mortality.[4]

These findings may therefore pave the way towards a more intensified and multimodal curative approach in young prostate cancer patients, especially those with lower competing mortality risk.

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DIFFERENTIATED THYROID CANCER: MANAGEMENT OF LOCALIZED DISEASE

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Differentiated thyroid cancer (DTC) is the most frequent endocrine tumor nowadays and presents mostly (90%) as papillary thyroid cancer and less as follicular one. The goals of treatment of DTC are to remove the primary tumor and minimize the risk of recurrence, without forgetting treatment-related morbidities.[1] DTC can present at diagnosis as operable or, less frequently, as inoperable disease.

For operable disease, surgery is usually the first step: hemi- or total thyroidectomy are performed considering tumor extension. Neck lymph node dissection can be added if lymph node metastases are clinically suspected. Guidelines stratify the administration of radioactive iodine (RAI) and the activity to use, basing on the probability of disease persistence or recurrence: for very low risk DTC - small tumors without evidence of extrathyroidal invasion or lymph node involvement - RAI is not recommended. On the other hand, high RAI activities become necessary in patients with aggressive histological and molecular characteristics, incomplete tumor resection, gross extrathyroidal extension, clinically positive lymph nodes. Across the spectrum of low and intermediate risk situations, patients should undergo RAI treatment with activities tailored considering risk factors for recurrence and if we expect need for remnant ablation or if instead undetected micrometastases presence is presumed.[2,3]

Inoperable disease not rarely leads to a direct tumor extension to surrounding organs: recurrent laryngeal nerve, larynx, trachea or esophagus. Surgery is still a cornerstone of management, with the aim of debulking or removing gross tumor, preserving as possible other structures. Then, post-surgery therapy should be offered: RAI is recommended in guidelines as in high risk patients, external beam radiotherapy (EBRT) can be considered to improve locoregional control, particularly in front of gross or microscopic residual disease in which additional surgery could be ineffective.[4,5] However, the evidence of effectiveness of EBRT in DTC is a matter of debate, since the lack of multicentric and prospective studies.[6] In patients not suitable for a safe surgery or with a rapidly progressive disease, options include EBRT and/or a systemic therapy. This remains a condition with high incidence of both locoregional and distant failure.

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THE MANAGEMENT OF METASTATIC DISEASE

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The prognosis of differentiated thyroid carcinoma (DTC) is generally favorable with 85% of newly diagnosed patients cured with surgery alone or in combination with I-131 radioiodine (RAI) therapy. However, recurrent disease occurs in up to 20% of patients and metastatic disease is found in 10-15% of cases.

Tumor burden, location of the metastatic lesions, and RAI avidity/refractoriness drive the therapy of metastatic DTC (mDTC). All these conditions affect the prognosis, which becomes severe (<10% in 10 years) in case of RAI refractory mDTC. Both systemic treatments and local therapy can be indicated. In RAI-avid disease, RAI therapy may prolong overall survival and disease-free survival. Generally, activity ranging from 3.7 to 11.1 GBq is used but an individualized approach could be employed in case of renal, lung or hematologic comorbidities as well as in pediatric patients. Long term toxicity affects salivary glands principally. Multiple courses of RAI therapy are possible until in presence of iodine sensitive disease but 50% of patients show or develop RAI refractory disease defined according to the criteria of the American Thyroid Association. Biological mechanisms of RAI refractoriness can be found in the impairment of Na/I symporter function, which can derive from alteration in signaling pathways involving several genes such as BRAF. In this scenario, active surveillance and TSH suppression can be sufficient in patients with limited disease and asymptomatic. Additionally, local approaches with surgery, external beam radiotherapy, stereotactic radiotherapy, ablation with radiofrequency or embolization should be taken into account. Data are limited but encouraging for surgery and radiotherapy and include mainly retrospective reports, which help clinicians to postpone the initiation of systemic therapies.

Nowadays few systemic agents are available and Tyrosine Kinase Inhibitors (TKi) represent the optimal strategy in patients with widespread, rapidly progressive and symptomatic disease. Among TKi, Lenvatinib showed a median PFS of 18.3 months in the SELECT trial. Unfortunately, TKi are burdened with severe side effects causing dose reduction and treatment discontinuation. Several options are available to manage mDTC to be administered alone or in combination, thus balancing oncologic results with side effects and impact on quality of life. A multidisciplinary discussion is mandatory to ensure the optimal treatment schedule.

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INNOVATION AND SUSTAINABILITY IN DIAGNOSTIC RADIOLOGY

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The talk will present the latest innovations in Diagnostic Radiology related to the new technologies developed in Ultrasound, Computed Tomography and Magnetic Resonance Imaging. It will consider the new softwares designed to improve the hospital patient journey, the execution of diagnostic imaging examinations and to accelerate the interpretation and reporting of imaging tests by radiologists. Another important recent novelty is the approval of a new high relaxivity macrocyclic gadolinium-based contrast agent that will reduce the gadolinium retention inside patients while maintaining the same diagnostic efficacy of previous contrast media. The speaker will go on debating all the sectors where the application of Artificial Intelligence systems is trying to provide accurate and automatic suggestions, starting from the selection of appropriate imaging requests and ending to patient explaining follow-up actions after specific findings on Imaging. But although this historical period is one of the most exciting, considering all the new applications in the field, we have to consider the sustainability of

diagnostic Radiology. The environmental impact of radiological activities is not negligible. Is important to consider the amount of energy that a Radiology department consumes and how we can reduce the Imaging carbon footprint without sacrificing patient care and safety. As diagnostic Radiology is a relatively high-cost and high-maintenance aspect of Medicine, a second item to take into account is that in developing and underdeveloped countries there is a clear deficiency or lacks of even basic Diagnostic Imaging. So it must be our duty to cooperate with international organisations to produce extending hands-on teaching to increase the number of skilled doctors in imaging interpretation. Diagnostic Radiology plays a unique role in healthcare practice, from disease diagnosis, expecially in an emergency setting, to prevention, surveillance and treatment monitoring, so it is critical to have an adequate number of practising radiologists. But in Italy, after a ten years period of reduction of financing of the National Health Service, an overuse of unappropriate imaging tests, some errors in planning the number of contracts for the access to diagnostic Radiology recidency, and more and more radiologists seeking jobs in private practice, we are recording a shortage of radiologists with an increasing workload in Diagnostic Imaging department that produces elevated turnaround time in reporting and raised waiting time for obtaining the appointment to perform a diagnostic imaging examination. The latter are the main challenges that Italian diagnostic Radiology need to solve to maintain its important role inside healthcare practice.

INNOVATION AND SUSTAINABILITY IN RADIATION ONCOLOGY

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Aims: To explore the major trends of the innovation in Radiation Oncology. To evaluate the affordability of these innovations.

Methods: The major trend of innovations were identified from the literature, the international research programs and by meetings with the industry of the fields.

Results: The major trends were related to IGRT and AI interaction to optimize already in the imaging simulation devices (CT/MRI) the collection not only of images, but also of the proposals and the dosimetric plans. Furhtermore, the same interoperabilty is becoming available in the treatment rooms based on optimized hybrid machine technologies. Another emerging trend is related to the omic integrazione the treatment choice and optimization. The evolution of the professional roles, the time of this processes and their affordability is also analyzed.

Conclusions: The challanges of innovation in the radiation oncology discipline is growing and the exploration of new clinical and operational paradigmes will be needed.

RADIOTHERAPY IN MULTIFOCAL OLIGOMETASTATIC DISEASE: NUMERICAL OR TECHNICAL LIMIT?

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The oligometastatic setting was defined in 1995 as an intermediate state between localized and widespread diffuse disease,[1] however it is nowadays considered as a heterogeneous setting that includes patients who differ from each other for several characteristics, including extension and timing of appearance of the metastatic disease. Recently, the ESTRO-EORTC consensus recommendation established a classification of these patients into subcategories according to 17 disease characterization factors and 5 different questions.[2] In the absence of validated molecular biomarkers, the oligometastatic setting is currently defined by the presence of a limited number of metastases, more commonly from 1 to 3 lesions.[3–6] Despite systemic therapy represents the standard of care for metastatic patients, Stereotactic ablative radiotherapy (SABR) emerged as an effective and safe option to treat patients with a limited number of metastases. Gomez *et al*.[7] evaluated the impact of local consolidative therapy in addition to standard of care in patients affected by 3 or fewer metastases from non-small cell lung cancer (NSCLC), showing a benefit both in progression free survival (PFS) (from 4.4 to 14.2 months, p=0.022), and in overall survival (OS) (41.2 months vs 17.0 months, p=0.017). A PFS benefit was demonstrated also by Iyengar *et al*.[8] in a study that included NSCLC patients with no more than 3 lesions in the liver or the lung. Nevertheless, delivering SABR in patients with multiple metastases still represents a challenge from both the clinical and technical points of view. It is debated if the limit to metastases' ablation should be numerical or related to the technical feasibility. Indeed, in the real-world data published by Chalkidou et al., among 1422 oligometastatic patients, only 4.8% were affected by 3 simultaneous metastases and no patients with 4 or 5 lesions.[9] With this background, we will discuss about the role of SABR for patients affected by multiple oligometastases.

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THE COMBINATION OF PARP INHIBITORS AND RADIATION THERAPY IN OVARIAN CANCER

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About 15-25% of high grade serous ovarian cancer are BRCA1/2 mutated. The inhibition of the poli (ADP-ribose) polimerase (PARP) is lethal in this kind of tumor through the so-called "syntetic lethality" mechanism.[1] Historically, the role of the radiation therapy in ovarian cancer has been limited by the late gastro-intestinal toxicity associated to the whole abdominal irradiation[2] and by the advancement in systemic therapy. Recently, however, the development of high precision technique of radiotherapy such as the intensity modulated and the stereotactic ablative radiation therapy has given new perspective to the radiation treatments. In selected disease scenarios (i.e. oligometastatic/persistent/recurrent disease[3]), adoption of stereotactic body radiotherapy is able to deliver high radiation doses to small volumes in few fractions (usually 3-5), and can be employed for curative-intent treatment strategies.[3-5] Additionally, stereotactic radiotherapy has low acute and late toxicities and can be used in reirradiation scenarios.[6] Moreover, stereotactic radiotherapy can be safely administered even during conventional systemic chemotherapy regimens,[7] because the short schedules can be conveniently inserted between one cycle and another. In this context, the association of new molecules, such as the PARP inhibitors, and the modern stereotactic irradiation could ameliorate the therapeutic index by a synergistic effect on tumoral cells. The biological rational of this approach has been demonstrated both in *in vitro* and in *in vivo* studies.[8,9] Clinical trials on human on this subject are very few,[10] especially in ovarian cancer and with unconventional radiotherapy fractionation. The preliminary results of the first Italian multicentric study "Epimetheo", which associated PARP inhibitors to stereotactic radiotherapy in oligometastatic/persistent/recurrent ovarian cancer, will be presented. In this clinical setting, our study confirms the efficacy and the safety in patients of stereotactic radiotherapy in association with PARP inhibitors. The toxicity rate in this series is consistent with that described in the literature about the stereotactic technique, and the addition of the PARP inhibitors do not worsen the toxicity.

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AGGRESSIVE MULTIMODAL APPROACH FOR OLIGOMETASTATIC BREAST CANCER PATIENTS IN THE ERA OF MODERN SYSTEMIC THERAPY

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About 50% of metastatic breast cancers (BC) patients present with few metastatic lesions and show long survival. These patients can be defined as oligometastatic in presence of 1-5 metastatic lesions safely treatable with local therapy.[1] Retrospective or prospective non-randomized studies highlighted a survival benefit in oligometastatic breast cancer (OMBC) patients treated with a multimodal approach which combines metastases-directed therapy (MDT), consisting of stereotactic ablative body radiotherapy (SABR) or surgery, and systemic therapy.[2] However, randomized studies showed conflicting results.[3,4]

Looking forward to additional randomized evidence we must consider that systemic therapy advancements in different BC subtypes are leading to significant survival improvements. The association of docetaxel, trastuzumab and pertuzumab raised the number of HER2-positive long-survivors[5] and the introduction of cyclin-dependent kinase 4/6 inhibitors revolutionized hormone receptor-positive BC treatment[6]. In this context an aggressive approach consisting of MDT in addition to these new systemic therapies could allow OMBC patients to reach long-term survival or even the cure. Moreover, the establishment of immune checkpoint inhibitors in metastatic triple-negative disease[7] further support a multimodal treatment, considering the synergistic effect between RT and immunotherapy.[8]

In conclusion, while waiting for other well-designed and disease specific trials, every OMBC patients should be discussed by a multidisciplinary team since we cannot miss the opportunity to reach long-term survival.

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MANAGEMENT OF OLIGOMETASTATIC PATIENTS CANDIDATE TO ABLATIVE RADIOTHERAPY

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Since the first definition in 1995,[1] oligometastatic (OM) disease has been extensively studied, both retrospectively and prospectively.

From "real life experience" we learned a lot, but many issues still need to be studied and clarified.

The clinical management of OM patient's candidate to ablative RT implies:

- Correct identification of OM state
- RT planning, balancing outcomes and side effects
- Integration with systemic therapies
- Ad hoc follow up after treatment

Concerning patients' identification, we should acknowledge that the definition of OM remains generic and almost unmodified since 1995.[1] Recent efforts conducted by ESTRO and ASTRO[2] did not end up with a more accurate definition, so OMD was still defined as 1-5 metastatic lesions, a primary controlled tumor being optional, but where all metastatic sites must be safely treatable. A parallel initiative by ESTRO and EORTC[3] contributed to creating a common language for OMD and identified nine possible subcategories of this state. This commendable work highlighted a common clinical obser-

vation: OMD is a very heterogeneous scenario, and the absence of reliable biomarkers for identifying it makes clinical results extremely variable.

However, major efforts are still required to improve our understanding of the disease biology. The multidisciplinary evaluation is crucial in this phase.

From a technical point of view, we cumulated significant experience on how to treat with ablative RT almost any lesion in any body site. However, there are still challenges that need to be addressed, such as treatment of multiple lesions of re-irradiation. Another rapidly evolving scenario that questions us as radiation oncologists is represented by "new" systemic therapies, such as target therapies and immunotherapy. Patients living longer thanks to these effective therapies are more likely to need one or more courses of ablative RT during their history. At the same time, there are other uncertainties concerning positive or negative interactions with RT. Clinical data about effectiveness and tolerability of such combinations are generally poor, so that clinical experience and practical compromises are often driving our daily clinical practice. Lastly, managing the follow up of these patients requires a direct involvement of a radiation oncologist with experience in the field of SBRT. Evaluation of response, as well as a prompt identification and management of rare but important side effects that could occur (for instance radionecrosis) again requires multidisciplinarity and expertise.

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STEREOTACTIC ABLATIVE RADIATION THERAPY IN OLIGOPROGRESSIVE METASTATIC PATIENTS

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The standard of care for metastatic cancer is systemic therapy, with radiation used for palliation of symptoms. Interestingly, a large proportion of patients enrolled in first-line metastatic cancer trials have a limited number of metastatic sites. Despite this, the outcome in terms of progression-free survival

(PFS) after a first line of systemic therapy is poor. Moreover, only 2% of patients that achieve a complete remission of disease after systemic therapy maintain a long-term response.[1] Treatment with the monoclonal antibodies and immunotherapy in addition to chemotherapy dramatically improved survival in some cohort of patients. A ''clinical significant state of oligometastases" has been defined to describe a clinical scenario in which a limited number of meta static sites might represent a state in which the full metastatic potential of cancer has not been achieved.[2] Based on this hypothesis, local treatments, including surgery or ablative radiotherapy, have been employed with the aim of achieving long term local control and possibly increasing the overall outcome.[3] Based on these observations, recent studies have investigated the possible role of ablative local therapies in oligometastatic cancer patients. However, the majority of the published studies were designed to assess the safety and efficacy of local radiotherapy only in terms of local control, without providing evidence of its effect on the overall outcome.[4] In the present lecture we wish to review the main published data on oligometastatic cancer patients treated with radical radiotherapy to all metastatic sites.

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ORGAN PRESERVATION AS PART OF CURRENT MANAGEMENT OF EARLY STAGE - LOW RISK RECTAL CANCER

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Aims: To present a narrative review of current evidence in organ preservation (OP) strategies in rectal cancer (RC) focusing on the role of this approach in early stage – low risk disease. Future perspectives in this field were also discussed.

Methods: Clinical trials evaluating OP strategies in RC were reported with a focus on outcomes of patients (pts) with early-low risk disease. The clinical challenges in improving this practice and the rate of pts receiving OP were discussed as well as the topic of quality of life evaluation.

Results: Total Mesorectal Excision, with neoadjuvant chemoradiation (NACRT) in locally advanced disease, is the standard of care in RC. This approach has significantly improved oncological outcomes but the reported rates of bowel, urinary and sexual disfunction were up to 25-30 per cent. Several trials investigated OP strategies after NACRT in order to minimize these effects and to improve pts quality of life. These trials evaluated different approaches, such as watch and wait (WW) and local excision (LE), and were different in selection criteria

either including pts only according to tumor response regardless of initial stage or preselecting pts according to initial tumor. These trials reported two important results: first, if a selection approach including an initial evaluation of tumor risk factors, an advanced evaluation of response and a selective choice of WW or LE based on respose was used the rate of OP was up to 60 per cent of pts who met the inclusion criteria; second, even though a tumor regrowth rate up to 30 per cent has been reported, salvage surgery was effective in the majority of pts. An important challenge in OP strategies is how to optimize tumor response. Several studies focused on increasing the interval between NACRT and surgery, intensifying radiotherapy or chemotherapy in Total Neoadjuvant Therapy approaches. Evidence regarding the use of immunotherapy are also emerging. Definition of clinical and radiological criteria for response assessment and its timing is also an important feature. One of the most important challenges still ahead is the assessment of quality of life which, while representing the primary goal of OP, is also the most difficult to report in a standardized way. The use of validated questionnaires and the evaluation of patient reported outcomes is needed to understand the real success of this approach.

Conclusion: OP is a promising approach in RC, mostly in early disease. OP optimization requires further investigation.

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COME MIGLIORARE GLI OUTCOMES NEGLI STADI SFAVOREVOLI

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Neoadjuvant chemoradiation therapy (nCRT) is the standard treatment modality in locally advanced, non-metastatic rectal cancer (LARC) patients, for whom the surgical margin is threatened, or the risk of local recurrence is increased. Based on MRI imaging, able to identify poor prognostic factors preoperatively, three prognostic's groups ("good", "bad" and "ugly") of rectal cancer patients, according to their local and systemic failure's risks, have been identified.[1] Several treatment's modalities as chemotherapy, radiation and surgery and their combination have been tested during the years to reduce the risk of local recurrence and distant metastasis. Total Neoadiuvant Therapy (TNT) with the administration of an induction or consolidation chemotherapy in association with chemoradiation prior to surgery for stage II/III rectal cancer before or after neoadjuvant radiochemotherapy has been tested with different agents and schedules.[2] The addiction of Oxaliplatin to the standard fluoropirimidine's neoadiuvant chemo-radiotherapy regimen, has been tested in several Randomized Clinical Trials with a controversial result in terms of pathologic complete response (pCR) and disease-free survival (DFS). Stating that, oxaliplatin added to standard chemoradiotherapy in patients affected by locally advanced rectal cancer seems to improve DFS and overall survival (OS) in patients < 60 years of age.[3]

Moreover, since response to RT is dose dependent in rectal cancer, dose escalation may lead to higher complete response rates and better DSF. Recently, an early tumour regression index (ERI) was introduced to predict pathological CR (pCR) after nCRT in LARC patients to predict patients who will achieve complete response (CR) during radiotherapy treatment, to be able to identify which patient could benefit most from a radiotherapy dose's intensification.[4]

Finally, the role of immunotherapy in colorectal cancer (CRC) has expanded, specifically in particular subsets of CRC, over the past few years. Novel biologics targeting the epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF) pathways have been the mainstay treatments for advanced or metastatic colorectal cancer (mCRC). Newer agents, such as programmed death-1 (PD-1) inhibitors have resulted in high efficacious results in particular subset of patients with microsatellite instability (MSI) as well as in a very specific group of CRC patients mismatch-repair deficient (5 to 10% of CRC) where a CR after 6 months of treatment was achieved.[5]

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UTILIZZO E TIMING DEI FARMACI DI PRECISIONE IN CORSO DI RADIOTERAPIA: RAZIONALE RADIOBIOLOGICO IN TERMINI DI EFFICACIA

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Concurrent administration of chemotherapy with radiation therapy is a standard practice since the 1980's. Combined modality therapy has several potential advantages, over radiation alone, to enhance tumor cell killing. Few prospective studies have evaluated the interaction between new targeted therapies (tp) and radiation therapy (RT), but available data are mainly based on retrospective experiences, often related to small sample sizes.

Aim of this relation is to discuss the radiobiological rational behind the possible association of tp and RT.

The most frequent and evaluated targeted drugs associated with RT are EGFR-inhibitors/TKI, HER2-inhibitors, BRAF/MEK-inhibitors, and VEGF-inhibitors.

EGFR inhibitors (EGFRi) promote RT-induced apoptosis, impair sublethal DNA damage repair, and affect the DNA-PK activity. Most frequently EGFRi used and explored with RT are Cetuximab/Panitumumab; they are monoclonal antibodies targeting EGFR, approved for RAS wild-type metastatic colorectal cancer and H&N cancers, and have demonstrated to be superior respect to CT-RT alone in selected patients with HNSCC. Other anti-EGFR currently used are Erlotinib and Osimertinib: small-molecule tyrosine-kinase inhibitors directed to VEGFR, PDGFR and Raf, indicated in NSCLC, renal cell carcinoma, and other cancer types. They can block tumor angiogenesis, cell division, and proliferation; moreover, Osimertinib has demonstrated to have an important intracranial activity. Evidences deriving from different clinical studies have confirmed that there are not evidences supporting the routinely concomitant integration of Erlotinib and RT; but promising clinical studies are ongoing on RT and Osimertinib. HER2 inhibitors show the ability to enhance radiosensitivity in breast cancer, and clinical data provide evidence of a good safety profile in the association with RT. BRAF inhibitors (BRAFi) act reducing lethal DNA damage repair, inducing cell cycle arrest in G1 and increasing RT induced apoptosis in cancer cells. The combination on RT and BRAFi has shown remarkable increases in treatment efficacy; nonetheless ECOG guidelines still recommend to hold 3 days before and after fractionated RT, 1 day before and after radiosurgery. VEGF-inhibitors (VEGFi) may enhance tumor responses to RT. Moreover, Bevacizumab, one of the first described VEGFi, has shown clinical and radiological improvement in patients with brain radiation necrosis and it has been recently approved for this indication.

In conclusions, target therapy and RT combination is a promising challenge for the near future, but available data are still limited: future clinical trials, with longer-term results, are needed to confirm both efficacy and safety of association.

TOXICITY OF NOVEL DRUGS AND RADIOTHERAPY: RADIOBIOLOGICAL RATIONALE

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Novel drugs such as targeted drugs (TDs) and immune checkpoint inhibitors (ICIs) represent a fundamental part of the actual cancer treatment armamentarium. Based on the molecular specificity, these drugs had significantly less side effects compared to chemotherapy. However, all of these agents have their specific side effects. Accumulating interest has emerged in exploring the toxicity profiles of the combination strategy of radiotherapy (RT) and TDs or ICIs. In fact the combination of these drugs with radiation harbours special risks and much remains unknown regarding safety and the potential increased risk of toxicity of a combined treatments. Nevertheless, combining these new drugs with the most advanced radiation technologies such as stereotactic body radiation therapy (SBRT) can represent an exciting development and challenge in the treatment of cancer patients.

Radiobiology mechanisms underlying interaction may explain the potential toxicities of these novel drugs given in combination with RT. The nature of RT-induced adverse events (AEs) based on the DNA damage of normal tissue, which is related with the dose delivered and volume irradiated and the tolerance of surrounding normal tissues may strongly be influenced by the addition of these novel drugs. To increase awareness of adverse effects and support immediate and successful management, the available literature on the safety of RT combined with newer drugs will be reviewed. Moreover underlying radiobiological mechanism will be explored in terms of radiation doses and fractionation, irradiated volume, timing of RT, potential biomarkers to predict tox-

icity. A number of important questions remain to be addressed, including dose/ fractionation regimens associated with damaging vs protective effects, the potential contribution of any novel drug on the development of radioresistance and the ability to reverse dose rate effects and induce hyper-radiosensitivity.

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RADIOBIOLOGY AND NEW DRUGS: FUTURE PERSPECTIVES

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The discovery and approval of innovative anticancer drugs in the last decade have revolutionized oncology treatment. Newer technical improvements in radiotherapy have also been rapidly implemented in recent decades, allowing an improved therapeutic ratio. A promising strategy to improve outcome of our patients is to combine these new drugs acting synergistically with radiotherapy. Fast-paced progress are specially focused on immunotherapies, targeted-therapies, anti-angiogenic treatment, DNA repair inhibitors, hormonotherapy and cell cycle inhibitors. The development of strategies using local and systemic treatments concurrently, mainly targeted therapies, has however stabilised.

In this review, key biological mechanisms, pre-clinical and available clinical data are discussed with the aim of identifying future precision drug–radiotherapy combinations.

RADIOTHERAPY–IMMUNOTHERAPY COMBINATIONS: BIOLOGICAL BASES AND OPEN CHALLENGES

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For decades, the rationale for using ionizing radiation to treat cancer has been attributed to its cytotoxic activity, in particular by inducing DNA damage eventually leading to cell death. This view of radiotherapy (RT) as a simple cytotoxic agent has radically changed in the past few years, and it is now widely accepted that RT can reshape the tumour environment, particularly by modulating the immune response. Indeed, in the last decade a large amount of preclinical data have been generated, demonstrating that radiotherapy can trigger both the adaptive and innate immune responses toward antitumor activity. Such evidence gave a strong rationale for the use immunomodulators to increase the therapeutic activity of RT (immunoradiotherapy), with several preclinical and some clinical positive results that have been obtained. Nevertheless, several points remain to be addressed, as the need to find biomarkers to identify patients who will benefit from immunoradiotherapy, and mechanisms to overcome resistance. Moreover, as the balance between stimulating and suppressive signals finely regulates the activity of the immune system, it is not surprising that together with immunostimulatory responses, RT can also trigger immunosuppression. Accordingly, we have shown that upon irradiation an influx of monocytes and regulatory T cells (Tregs) into the tumour, which are recruited via the CCL2/CCR2 pathway, restrains the antitumor efficacy of RT. We have also dissected the role of transforming growth factor (TGF)beta-mediated immune suppression after RT, identifying a novel mechanism that involves the inhibition of type I interferon production by myeloid cells. Such observations suggested novel therapeutic approaches to counteract the RT-induced immunosuppression and we demonstrated, using different murine orthotopic models of lung and oral cancer, that inhibitors of CCR2 and TGFbeta receptor increased the efficacy of RT, paving the way for potent combined radio-immunotherapies.

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OXYGEN-GUIDED RADIOTHERAPY

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Radiotherapy is an essential component of cancer treatment in roughly 50% of patients diagnosed with cancer.[1] However, radiotherapy treatment does not always achieve a satisfactory response to all treated lesions, both in curative and palliative settings.

In addition to the intrinsic radiosensitivity of tumor cells, the presence of hypoxia in the tumour microenvironment (TME) is one of the leading causes of radio- and chemo-resistance.[2] Hypoxia has been recognized as a key component of the TME and is considered a major cellular stress factor that affects a wide range of molecular pathways.

There are mainly two aspects by which hypoxia leads to resistance to radiotherapy. In contrast to normal blood vessels, the tumor vasculature includes an aberrant and chaotic network of new vessels, resulting in an inadequate vasculature that impairs the direct interaction of ionizing radiation with oxygen (oxygen fixation hypothesis).[3] Furthermore, hypoxic areas release several mediators that promote neoangiogenesis, inhibition of apoptosis, immune suppression, changes in the metabolism of cancer cells, and tumour microenvironment (TME).[4,5] Once the oxygen concentration is around 2% or below, the hypoxia-related pathways are activated by a family of transcription factors, the hypoxia-inducible factors (HIFs).[2,6] The resulting tumour adaptation is characterized by drastic changes in gene expression patterns that allow cells to survive in a hostile and oxygen- and nutrient-poor environment. Unfortunately, these changes also give the tumour increased aggressiveness and the tools to resist cancer treatments.

In order to improve the efficacy of radiotherapy, hypoxia is considered one of the major challenges to be faced, so there is an expanding field of studies aiming to explore strategies to radiosensitize hypoxic tumours. Those efforts involve approaches such as increasing oxygen supply, hypoxia-activated drugs, anti-angiogenic agents, or hypoxia-targeted therapies [2]. However, currently, there is not a satisfactory state of the art in treatment for hypoxia in cancer patients. Moreover, translational research aiming to identify patients with a hypoxic tumour suitable for an anti-hypoxic strategy is still lacking.

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SPATIO-TEMPORAL FRACTIONATION

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In recent years, radiotherapy is becoming a biology-driven discipline. The ever increasing evidence of the importance of the so-called 'non-targeted' effects on the biological response to radiation, such as cell signalling effects, the role of the vascular, stromal and immunological changes induced in the tumour and its microenvironment by the radiation, is leading to a paradigm shift in radiotherapy. Temporal schemes using very high-dose radiation in one fraction could transform the immunosuppressive tumour microenvironment, resulting in an intense CD8 T-cell tumour infiltrate. Very high-dose rates (>40 Gy/s), as those employed in FLASH therapy, among other effects, appear to prevent both activations of the TGF-β/SMAD cascade and acute apoptosis in blood vessels, resulting in a significant gain in normal tissue tolerances. Moreover, there is biological evidence suggesting that additional therapeutic gain may be achieved if we allow for temporal variation in the radiotherapy plan. This treatment paradigm is known as spatiotemporal fractionation (SFRT), that is delivering distinct dose distributions in different fractions. These dose distributions are designed such that different fractions deliver high single-fraction doses to complementary parts of the tumor while achieving a similar dose bath in the surrounding normal tissue, thereby increasing the biological effect in the tumor while exploiting the fractionation effect in the normal tissue. SFRT uses a combination of spatial fractiona-

tion of the dose and narrow beams. The utilisation of distinct spatial distributions activates different biological mechanisms from those involved when direct damage by ionizing radiation takes place. There are four main types of SFRT: GRID therapy, LATTICE therapy, microbeam radiation therapy and minibeam radiation therapy. One of the main differences among them is the geometry and size of the beamlets. The main potential biological mechanisms are differential vascular effects in the normal versus tumoural tissues, cell signalising effects (bystander-like effects/abscopal effects), inflammation and immunomodulatory effects, migration and proliferation of stem cells to repair the tissue, free radical production and diffusion. The lesson being taught by SFRT and FLASH therapy is that the exploration of how the physical parameters of the irradiation modify the biological response can offer enormous opportunities for optimal patient treatments.

PLAN QUALITY IN STEREOTACTIC RADIOTHERAPY: THE MEDICAL PHYSICIST POINT OF VIEW

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The concept of plan quality encompasses so many different aspects that a global consensus on the metrics to be used is difficult to find. From the medical physicist's point of view,[1] three main aspects will be discussed: dose distribution, robustness, and complexity of treatment plans.

Dose distribution evaluation is considered the most relevant aspect of plan quality assessment. However, as protocols and requirements may also depend on habits and preferences, this assessment is not straightforward. Prioritization of dose objectives and constraints on targets and organs at risk is the starting point for further evaluations that involves inspection of slice-by-slice dose maps and evaluation of dose-volume histograms. Metrics such as plan homogeneity, plan complexity and gradient indices are used to assess the dose distribution quality. Furthermore, as it may be practical to combine all this information into a single quality index, several authors have proposed a composite score.[2-4]

Regarding the robustness of the plan, several strategies can be used to account for uncertainties due to patient positioning and/or target movement. The traditional and most common approach is to set margins around the clinical target volume to define a larger volume used during planning. This strategy, however, does not always guarantee adequate dose distribution. The alternative is the so-called "robust planning", where uncertainties are managed during plan optimization by considering several possible patient position/movement scenarios.[5] Finally, regardless of whether the plan was optimized using the traditional or the robust optimization method, it is always possible to assess the robustness of the plan a-posteriori.

The objective of assessing the complexity of a stereotactic intensity-modulated treatment plan is to identify possible dosimetric uncertainties (due to small and irregularly shaped beam segments) and difficulties in plan delivery (due to the high level of modulation of machine parameters). Although a certain degree of complexity is necessary to ensure good dose conformity,[6,7] some researchers report that treatment planning systems sometimes propose plans with an unnecessarily high degree of complexity. It is worth remembering that a high-quality plan does not necessarily imply a plan with a high degree of complexity.[8]

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EVALUATION OF THE DOSE TO THE TARGET

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Aims: The evaluation of plan quality is a key step in the workflow of radiotherapy. This is particularly relevant when high dose per fraction is delivered in few fractions with abrupt dose fall off, as in stereotactic radiotherapy.

Methods: At first, it is important to agree on the definition of plan quality and the parameters it depends on. Plan quality in radiotherapy needs the clinical suitability of the delivered dose distribution that can realistically be expected from a treatment plan.[1]

Results: The normal plan quality assessment relies on the evaluation of the dose distribution calculated by the treatment planning system. The evaluation of the 3D dose distribution is not trivial, as it may be difficult to assess its spatial characteristics and its specificity with respect to individual patient characteristics. Furthermore, the calculated dose distribution does not exactly correspond to the dose delivered to the patient due to uncertainties in the dose calculation and the treatment delivery, including variations in the patient set-up and anatomy. Therefore, plan quality also depends on the robustness and complexity of the treatment plan.[2]

Conclusions: Future work and consensus on the best metrics for quality indices are required and better tools are needed for the evaluation and reporting of dose distributions, plan robustness and complexity.

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ORGANS AT RISK (OARS) EVALUATION

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Aims: The evaluation of the quality and dosimetric efficacy on the organs at risk (OARs) in Stereotactic Body Radiotherapy (SBRT) is based on multi-criteria optimization (MCO). In order to achieve the disease control, while reducing the risk of toxicity and complications, SBRT dose and fractionation schemes vary according to lesion size and site, OARs proximity and the biological effective dose of each treatment schedule. Furthermore, SBRT requires special care in prescribing, recording and reporting. OARs quality aspects in SBRT are analyzed.

Methods: A survey of all the tools for the evaluation of standardized and updated constraints of OARs in SBRT together with the emerging dosimetric predictive models of toxicity was carried out.

Results: The research showed a broad and comprehensive spectrum of dosimetric metrics on OARs and SBRT quality plan evaluation. It is possible develop risk maps of Dose-Volume Histograms (DVHs), containing a subplot for each specific OARs volume, assembling and summarizing all data on constraints and integrating the AAPM 101 Report constraints, British consensus on SRT constraints and ICRU Report 91 parameters. This allows to enable stratified risk comparisons as a function of dose, fractionation and volume prescribed. Moreover, automatic plan generation and dose prediction using machine learning (ML), named knowledge-based planning (KBP) methods, provide an excellent opportunity for streamlining the treatment planning quality and workflow.

Conclusions: Beyond the standardized and known dose constraints, it is necessary to introduce new integrated models into clinical practice to evaluate their promising potential and enhance the therapeutic index of SBRT treatment planning.

LA RESPONSABILITÀ PROFESSIONALE

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Necessaria una legge che definisca l'atto medico, anzi "il ruolo medico. Certamente positivo, anche se esistono criticità di natura applicativa e interpretativa, il giudizio sulla Legge Gelli. Ricerca per dare un assetto normativo di riferimento ad una materia che in questi anni, per le dimensioni del contenzioso, ha assunto una rilevanza sempre più importante. Si è cercato di uniformare le prassi e le linee comportamentali che caratterizzano la professione sanitaria, mediante la validazione dei criteri e delle regole da parte dello Stato; regole e linee guida validate dalla comunità.

La responsabilità, quale essenza stessa della professionalità e della potestà di curare, è il pilastro fondante della autonomia del medico nelle scelte diagnostiche e terapeutiche che, fatti salvi altri diritti e doveri costituzionali, in primis il consenso informato, è stata più volte richiamata dalla Suprema Corte come tratto incomprimibile dell'attività medica e ribadita in giudizi di merito e legittimità. L'autonomia nelle scelte diagnostico-terapeutiche e tecnico professionali e l'attribuzione delle connesse responsabilità, concorrono a definire quella posizione di garanzia che lo Stato riconosce ai medici. Le assicurazioni, rese obbligatorie dalla legge Gelli. dovranno essere regolamentate dal decreto attuativo che determini i requisiti minimi delle polizze per le strutture sanitarie e sociosanitarie pubbliche e private e per gli esercenti le professioni sanitarie, prevedendo l'individuazione delle classi di rischio a cui far corrispondere massimali differenziati. Molti professionisti sanitari nell'attuale sistema non riescono ad ottenere un'adeguata copertura assicurativa sul mercato per i costi eccessivamente alti delle polizze. In Italia i professionisti della sanità devono confrontarsi tutti i giorni con la paura delle aggressioni, delle denunce e delle conseguenze economiche e professionali che derivano da liti nella maggior parte dei casi temerarie, ciò in quanto il 95% di queste cause finisce in un nulla di fatto".

SIB IMRT, PREMISES AND RESULTS

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The SIB IMRT technique was first introduced for the treatment of head and neck cancers in 1999.[1] It has since spread in use, mainly employing moderately accelerated fractionation. The premises that led to its diffusion are a relative radiobiological advantage due to the reduction of the total treatment time, the best dosimetric profile and comfort for patients and the organization of radiotherapy departments. Scientific evidence relating to the comparison between sequential-IMRT and SIB-IMRT is scarce. [2,3,4,5]

In particular, it is not clear whether the toxicity profile can be equivalent or better and whether the conversion of dose constraints to EDQ2 is a sufficient and safe method to convert treatment plans with sequential IMRT with conventional fractionation into SIB IMRT plans with moderate hypofractionation. At the moment the SIB technique represents a treatment chosen mainly for its convenience, future studies will have to better elucidate the complex correlations between 3D dose distributions, clinical variables and outcomes.

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ROLE OF RADIOTHERAPY IN THE MANAGEMENT OF BLADDER CANCER: FROM PALLIATION TO CURE

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Despite advances in surgery, radical cystectomy remains mutilating, especially if orthotopic neobladder reconstruction is not feasible (> 50% of the cases), and thus negatively impacting quality of life. Furthermore, surgery is not an option in almost 50% of patients due to age and comorbidities. For such patients, trimodal treatment via transurethral maximal resection of the bladder (TURBT) followed by concomitant chemoradiation has emerged in recent years as a valid therapeutic alternative. Five-year control rates with bladder sparing associated with this strategy have been reported in the range of 40 to 65%, depending on the stage, leading to a 5-y OS rates of 40 to 50%, with excellent quality of life [9–22]. These results appear comparable to surgery [23]. Therefore, conservative trimodal therapy may be offered in highly selective and operable patients, i.e. patients with limited cT2 and unifocal tumours, without hydronephrosis or carcinoma in situ, with macroscopically complete resection of the lesion prior to initiation of concomitant chemoradiation. Radiotherapy may be also indicated for symptomatic or haemostatic purposes in case of metastatic or locally advanced tumours without the option of curative treatment (pain, haematuria, etc.), as well as in case of pelvic recurrence, either local and/or nodal.

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THE RADIOBIOLOGY OF RE-IRRADIATION AND CLINICAL APPLICATIONS

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Aims: Cancer survivors are at increased risk of developing secondary malignancies or localized disease recurrence within or close to original gross tumor volume; moreover, the improvements in radiation techniques have increased the confidence for reirradiation local recurrences. Re-irradiation is often characterized by a narrow therapeutic window and the potential for decreased efficacy and increased toxicity, especially if the cumulative total dose from both courses is high.[1]

Methods and results: Factors to consider before proceeding with a reirradiation are several, it is necessary to evaluate the restoration of normal tissue tolerance, the goal of the treatment, the available techniques, the prescription dose and the risk of severe toxicity of the second treatment (Table 1). A first step is to calculate the expected dose received from the previous course of radiation to all normal structures in the volume expected to be irradiated, this could be done using isoeffect metrics, such as EQD2 model with alpha/beta values of 10Gy for early reactions and 3 Gy for late reactions, in place of physical

dose to evaluate the total toxic effect in the involved OARs. In the re irradiated volume, it is important to divide OARS in early and late reacting as the degree of recovery varies with time and depends on the initial dose given and on type of OAR. Preclinical and clinical data indicate that the capability for long-term recovery from radiation injury may vary considerably among OARs and outcomes. Early responding tissues typically recover from radiation damage almost completely within a few months. For late toxicity, several organs including the heart, bladder, and kidneys did not exhibit long-term recovery, whereas the skin, mucosa, lung, and spinal cord did.[2] Spinal cord has been studied most extensively with regard to retreatment. In adult animals, restitution starts with a delay of several months and reaches a maximum of ≈140% of the original tolerance after 5–6 months. Woolley et al. proposed a model to estimate the spinal cord residual tolerance doses for elapsed times ranging from 70 days up to three years after the initial course of treatment.[3]

Conclusions: Clinical data supports RT as a treatment option for patients with recurrent or second tumours. However, if tolerance has already been exceeded, no re-irradiation is possible without loss of function; risk of normal tissue damage and impact on quality of life must be considered.

Table 1. Factors to consider for reirradiation.

Patient	PS Comorbidity Prognosis Toxicity from previous RT
Disease	Histology Site (in field, out field, border field)
Previous RT	Total dose Dose/fraction Time from first treatment Concomitant systemic therapies
Goal	Curative *vs* palliative
Other	Type of involved OARs
Delivery	EBRT, Brachytherapy, SBRT, hadron therapy

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RADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER

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Radiation therapy has been used for the past 50 years in the treatment of locally advanced pancreatic cancers (LAPC). In fact, following the publication of the GITSG trial,[9] for at least two decades the standard treatment of LAPCs was concurrent chemoradiation (CRT) based on 5-FU first and subsequently on gemcitabine. However, after the publication of the SCALOP trial results (6,10), capecitabine was considered the drug of choice in the CRT of LAPC.

A number of studies compared the results of CRT with those of chemotherapy alone[2-4,7,8] Some of these showed a significant improvement in overall survival in patients undergoing CRT (4.8) while other trials recorded similar outcomes between the two treatments[7] or better survival in patients undergoing chemotherapy alone.[2] Finally, a meta-analysis showed better survival rates at 6 and 12 months after CRT, but no significant differences at 18 months.[3] Based on these conflicting results, the role of upfront CRT in LAPC is still undefined. However, in patients with poorly controlled pain or local invasion with bleeding, upfront treatments based on radiotherapy can be considered as therapeutic options.[11]

CRT has also been proposed as a local consolidation treatment in patients with stable LAPC after a few courses of chemotherapy. However, the LAP-07 study did not record a significant improvement in patients undergoing this treatment although a reduced risk of local progression of LAPC was recorded in those undergoing CRT.[5]

Stereotactic body radiation therapy (SBRT) is an emerging modality in the local treatment of LAPC. The main theoretical advantages over CRT are the shorter duration of treatment, and therefore easier integration with systemic treatments, and the lower haematological toxicity, and therefore a potentially improved immunological profile. A case-control study comparing CRT and SBRT showed similar results in terms of overall survival, progression-free survival, and acute and late toxicity. However, patients undergoing SBRT experienced a statistically significant improvement in local control.[1] Furthermore, a meta-analysis, also aimed at comparing the same treatments in LAPCs, showed a higher 2-year survival rate and lower incidence of acute toxicity in patients undergoing SBRT.[12]

Further studies are needed to improve the contribution of radiotherapy in patients with LAPC. The purposes of these studies should be: i) to identify patients who can benefit from the integration between systemic treatments and radiotherapy; ii) identify the patients who can benefit most from one of the two radiotherapy techniques (CRT *versus* SBRT); iii) to thoroughly evaluate the possibility

Table 1. Results of the main trials.

Authors/year	Method	Main findings	Other findings
Moertel CG et al. 1981 (GITSG trial)	**Phase III** RCT comparing split-course RT alone (60 Gy) with split course CRT (40 Gy or 60 Gy)	CRT (40 or 60 Gy) was superior to RT alone (60 Gy)	No significant differences between CRT doses (40 versus 60 Gy)
Klaassen DJ et al. 1985 (ECOG trial)	**Phase III** RCT comparing 5-FU alone with RT (40 Gy) plus concurrent and adjuvant 5-FU 5-FU	The median OS was similar for both treatment programs as follows: 5-FU, 8.2 months; 5-FU plus RT, 8.3 months.	Severe or worse toxicity experienced by patients treated with 5-FU alone was 27%, and in the combined modality arm was 51%
GITSG 1988	**Phase III** trial comparing OS after multidrug chemotherapy (SMF) versus 5FU-based CRT followed by SMF	An improved median OS for the combined CRT plus CT (42 weeks) compared with CT alone (32 weeks) was demonstrated (p< .02).	/
Chauffert B et al. 2008 (FFCD-SWFO trial)	**Phase III** trial comparing CRT (60 Gy plus 5-FU and CDDP) followed by maintenance GEM with GEM alone	Median OS was shorter in the CRT than in GEM arm (8.6 and 13 months, p: 0.03)	More G 3-4 toxic effects were recorded in the CRT arm
Loehrer PJ Sr et al. 2011(ECOG trial)	**Phase III** trial comparing RT plus concurrent GEM versus GEM alone in LAPC	OS was 9.2 months and 11.1 months for GEM alone and GEM plus RT, respectively (p: 0.017)	G 3-4 toxicities were similar (77% [GEM] versus 79% [GEM plus RT])
Chen Y et al 2013	**Meta-analysis** comparing CRT with RT or CT for LAPC	CRT was superior in 6- and 12-mo OS to RT alone or CT alone group; the 18-mo survival showed no significant difference	CRT may increase treatment-related toxicities
Mukherjee S et al 2013 (SCALOP trial)	**Phase II** RCT comparing GEM- versus CAP-based CRT after induction CT	Median OS was 15·2 months in the capecitabine group and 13·4 months in the gemcitabine group; p=0·012	More patients in the GEM group than in the CAP group had grade 3-4 haematological toxic effects (18% vs o%, p=0·008)
Hurt CN et al. 2015 (SCALOP trial)	**Phase II** RCT comparing GEM- versus CAP-base CRT after induction CT	HRQL data support the use of CAP- over GEM-based chemoradiation.	There is deterioration in HRQL following CRT; this resolves within 3 weeks.
Hammel P et al. 2016 (LAP-07 trial)	**Phase III** RCT to assess whether CRT improves OS in LAPC controlled after 4 months of GEM-based induction CT	Median OS was not significantly different between CT (16.5 months) and CRT (15.2 months)	CRT was associated with decreased local progression (32% vs 46%, p: .03) and no increase in G 3-4 toxicity, except for nausea.
Arcelli A et al. 2020 (Paula-study)	**Case-control** study to compare CRT and SBRT in LAPC	No statistically significant differences in terms of acute and late toxicity, PFS, and OS were recorded among the two cohorts.	Median, 1-, and 2-year LC was: 16.0 months, 53.1%, and 40.5% in the CRT cohort and 22.0 months, 80.4%, and 49.8% in the SBRT cohort, respectively (P: .017).
Tchelebi LT et al. 2020	**Meta-analysis** to compare CRT and SBRT in LAPC	SBRT for LAPC may result in a modest improvement in 2-year OS with decreased rates of acute grade 3/4 toxicity and	no differences recorded in 1-year-OS or late toxicity.

Legend: 5-FU: 5-fluorouracil; CAP: capecitabine; CDDP: cisplatin; CRT; chemoradiation; CT: chemotherapy; G: grade; GEM: gemcitabine; HRQL: health-related quality of life; LC: local control; RT: radiotherapy; LAPC: locally advanced pancreatic carcinoma; OS: overall survival; PFS: progression-free survival; RCT: randomized controlled trial; SBRT: stereotactic body radiation therapy; SMF: streptozocin, mitomycin, and 5-fluorouracil.

of improving the resectability of LAPCs using radiotherapy in combination with systemic treatments; iv) to further evaluate the possible contribution of radiotherapy in improving the quality of life in these patients.

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"STORY TELLING" OF THE SPECIALTY IN RADIOTHERAPY. EDUCATIONAL NEEDS AND ATTRACTIVITY

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Radiotherapy, often named "Radiation Oncology", was defined by the International Atomic Energy Agency (IAEA) in 2009[1] as the discipline of clinical medicine that uses ionizing radiation either alone or in combination with other modalities for the treatment of patients with malignant or other diseases. As a matter of fact, several disciplines contribute to the knowledge of Radiation Oncology including basic and applied sciences, clinics, technology, and humanities.

In Italy, the educational program for Radiotherapy is based on two national laws: DM 68/2015 as far as the content and the organizational aspects and the DL 402/2017 as far as teaching requirements, clinical standards, and indicators for training activities.

Recently, several changes have been proposed to the "Osservatorio Nazionale per la Formazione Medico-Specialistica" by the Italian Board of Professors (MED/36) in order update the skills in relation to the biological, clinical, and technological progresses, also considering the needs of the context of the national health system.

In this regard, the European Society for Radiotherapy & Oncology (ESTRO) in 2019 published the "Recommended ESTRO Core Curriculum for Radiation Oncologists/Radiotherapists"[2] and the Italian Board of Professors of the "Settore Scientifico-Disciplinare di Diagnostica per Immagini e Radioterapia" (MED/36)drew up a document about the Core Curriculum for residents in Radiotherapy in 2021. Both these documents consider the Bloom taxonomy, reviewed in 2001,[3,4] which describes six levels of learning outcomes including knowledge, comprehension, application, analysis, synthesis, and evaluation, and the seven competencies of CanMED (medical expert, communicator, collaborator, leader, advocate, scholar, professional),[5] which are essential requirements that should be fulfilled by residents to became "Radiation Oncologists".

Despite the efforts to update and optimize the education and training of the residency programs in Radiation Oncology, the level of attractivity of this specialty for medical students is relatively low when compared to others. There are probably many reasons to explain this fact, including the limited exposition to the radiation oncology discipline in several academic programs during the medical school, the relatively limited number of radiation oncology departments in the country compared to other disciplines, and the scarce opportunity to exercise the free profession in private practice.

In the end, the Academic Institutions, the Scientific Society (AIRO) and the Politics should oversee the training programs, make choices, and take decisions to optimize the education of new specialists in Radiation Oncology who will have available more and more sophisticated and powerful tools, but should be consciousness of that and able to understand opportunities and risks.

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VERTEBRAL INSTABILITY AND THERAPEUTIC ALGORITHMS

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Advances in systemic therapy have increased the number of patients requiring treatment for spine metastases each year. Pain, with or without underlying instability, and neurological dysfunction secondary to metastatic epidural spinal cord compression are the primary indications for intervention. Spinal stability was defined as the ability of the spine under physiologic loads to limit patterns of displacement so as not to damage or irritate the spinal cord and nerve roots and, in addition, to prevent

incapacitating deformity or pain due to structural changes. Conversely, instability was defined as referring to excessive displacement of the spine that would result in neurologic deficit, deformity, or pain. Instability can be classified as acute or chronic, and the acute one has been further subcategorized as overt versus limited. A simpler conceptual approach would be to think of instability as overt, anticipated, or covert. From an oncological point of view, a classification system for spinal instability in neoplastic disease was developed by the Spine Oncology Study Group based on a systematic review and modified Delphi criteria evaluating factors crucial for the assessment of spinal stability. Six components of spinal instability are scored (pain, type of lesion, location, radiological alignment, radiological collapse, posterior element involvement), with the final Spine Instability Neoplastic Score (SINS) representing a composite score of the individual components. The score stratifies patients into three categories: those with a suspected stable spine (score 0 to 6), potentially unstable spine (score 7 to 12), and unstable spine (score 13 to 18). According to this classification, a surgical consultation is recommended for patients with SINS scores greater than seven. The sensitivity and specificity of SINS for potentially stable and unstable lesions is 95.7% and 79.5%, with a high intraobserver reliability.

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RUOLO DELLA RADIOTERAPIA STEREOTASSICA?

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The most frequent type of bone metastases are spinal metastases, which are thought to occur in 40% of patients with bone metastases. For a more appropriate treatment of patients with spinal metastases, the multidisciplinary approach is fundamental. We can categorize patients with spinal metastases and select the best treatment using a variety of methods, such as NOMS, a tool for determining the best multidisciplinary management of spinal lesions. Radiation therapy was initially used to treat spinal metastases in order to relieve discomfort. However, the goal of ablative therapy has been accomplished thanks to technological advancements, including the creation and use of stereotactic body radiation therapy. This made it possible to achieve not only the goal of pain resolution but also the possibility of delivering treatments with an ablative purpose. The choice of stereotactic radiation treatment, whether in a single session or with a hypofractionated scheme, depends on several factors related to the patient and the nature of the lesion to be treated. How therefore can we select the most suitable patient for stereotactic radiotherapy? To choose the best patient, we use a variety of guidelines from different scientific bodies. Furthermore, stereotactic radiotherapy could be used to treat patients who have already had neurosurgery in a postoperative scenario, or on patients who have already had radiotherapy in a reirradiation setting. My presentation will focus on these and other aspects of using stereotactic radiation to treat spinal metastases.

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DE-ESCALATION DOSE/VOLUME OF CONCURRENT RADIO-CHEMOTHERAPY IN HPV-POSITIVE OROPHARYNGEAL CARCINOMA

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Human papillomavirus (HPV) is now established as the principal cause of increased incidence of head and neck squamous cell carcinoma. HPV-related oropharyngeal squamous cell carcinoma (OPC) patients have a better prognosis but often suffer from long-term treatment-induced toxicities. The TNM 8th edition classifies OPC in HPV+ and HPV- tumors with differences both in T and N classification. Table 1 resumes OPC TNM staging.

Table 1. (TNM Clinical Classification).

Oropharynx p16 negative	Oropharynx p16 positive
Stage 0 Tis N0 M0	Stage 0 Tis N0 M0
Stage I T1 N0 M0	Stage I T1-T2 N0-N1 M0
Stage II T2 N0 M0	Stage II T1-T2 N2 M0
Stage III T3 N0 M0	T3 N0-N2 M0
T1-T3 N1 M0	Stage III T1-T3 N3 M0
Stage IVA T1-T3 N2 M0	T4 Any N M0
T4a N0-N2 M0	Stage IV Any T Any N M1
Stage IVB T4b Any N M0	
Any T N3 M0	
Stage IVC Any T Any N M1	

T – Primary Tumour; TX Primary tumour cannot be assessed; T0 No evidence of primary tumour; Tis Carcinoma in situ.

Several studies showed that HPV-related OPC was associated with significantly improved outcomes, including overall survival (OS). Some retrospective analyses on this issue demonstrated equivalent oncological outcomes in patients submitted to de-escalated radio-chemotherapy (RT-CT) (54-60Gy) compared to standard treatment (66-70Gy). Clinical trials evaluating de-intensification dose radiotherapy concurrent with biotherapy obtained poorer outcomes with respect to RT-CT; some studies on concomitant de-escalated radiotherapy plus immunotherapy are ongoing. De-escalated RT showed a low incidence of Grade3 toxicities, a minor incidence of prolonged use of PEG-tube, and better results in terms of quality of life (QoL) based on composite score (jaw-related problems, pain, social contact, eating, speech, and swallow). Finally, de-escalation dose/volume in OPC HPV+ patients can be considered a promising approach. Despite the evidence that radiation dose deintensification may improve long-term function in long-term survival OPC p16+ patients, more studies are needed on this issue. In fact, the majority of clinical trials have been single-arm phase II and need to be compared with the standard treatment in prospective randomized studies.

DE-INTENSIFICATION IN HPV+ OROPHARYNGEAL CARCINOMA: TREATMENT DE-ESCALATION AFTER SURGERY

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Aims: Human Papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC) shows better prognosis and higher response rates to radiotherapy (RT) and chemotherapy (CHT) compared to its HPV-negative counterpart. Concurrent CHT-RT often carries heavy long-term sequelae which may significantly worsen the quality of life (QoL) of patients that are normally young, healthy and with a long life expectancy. Efforts have been made to lower treatment side effects while keeping high disease control rates. In this scenario, transoral robotic surgery (TORS) and transoral laser microsurgery (TLM) turned out to be less toxic and as effective as open techniques when treating early stage diseases. This work aims to summarize and discuss the available evidence and the recent advancements in the field of adjuvant treatment de-escalation of HPV+ OPSCC.

Methods: A review of the literature, focusing on de-escalated treatment of HPV+ OPSCC in the post-operative setting, has been conducted.

Results: Several phase II trials have been designed, with different de-escalation strategies: 1) lower RT doses, 2) lower CHT doses; 3) smaller RT target volumes, 4) no CHT, 5) no RT. Not every single trial specifically required TORS or TLM. Pathological criteria defining low, intermediate and high risk patients differed as well. Recently, biomarkers such as circulating DNA or intra-treatment imaging response have been introduced to guide patients selection. Available results were different either in terms of disease control or in terms of QoL. Outcomes for TORS followed by standard adjuvant CHT-RT were poorer compared to those of standard definitive CHT-RT. Mild dose de-escalation ended up with no differences in terms of QoL. In selected patients, both aggressive dose de-escalation and avoiding RT on prima-

ry tumor site led to similar results as historical controls while achieving better QoL.

Conclusions: De-intensified therapies for HPV+ OPSCCs mean more precise and personalized treatments. Results from some of these trials might be encouraging. However, lack of homogeneity in risk criteria definition, RT and CHT dose reduction and/or omission, and even surgical approaches, makes it difficult to compare those trials. Even when disease control is maintained, attention must be paid to the actual gain in terms of QoL. So far, caution must be observed when adopting de-intensified treatments in clinical practice, and current standard of care should be routinely followed.

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OVERALL TREATMENT TIME: RADIOBIOLOGICAL ASSUMPTIONS AND CLINICAL IMPLICATIONS

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Good clinical practice dictates that radical courses of radiation therapy (RT) treatment should not be interrupted. However, RT treatment interruptions commonly occur, determining prolonged overall treatment time (OTT). The effects of OTT on the therapeutic efficiency of RT, extensively discussed in the literature, vary considerably depending on several factors, including tumor type, tumor characteristics, extent of delay and the radiation schedule. In general, it is thought that accelerated repopulation of RT surviving tumor cells during these protracted intervals is responsible for the inferior results of the treatment. However, recent radiobiological evidences indicate more complex mechanisms, including prolonged OTT-induced selection and enrichment of the radioresistant cancer stem cells. Thus, compensatory treatments are required to retain or limit the extension of the OTT, as much as possible but, despite several format for performing radiobiological compensations have been recommended, often pragmatic and non-radiobiologically justified approaches are used. This presentation aims to analyze the main radiobiological mechanisms through which a prolonged OTT and/or its incorrect management can favor RT failure and to provide practical tools to: i) identify the types of cancer most affected by treatment interruptions; ii) indicate the minimum duration of an interruption capable of having a significant effect on local tumor control; iii) classify patients according to the urgency to activate compensatory procedures; ii) list the recommended format for performing radiobiological compensation. Finally, we present a "homemade tool" for rapidly calculating the dose per fraction ideally needed to compensate prolonged OTT and the feasibility of its use in terms of toxicity and compliance with dose constraints.

MANAGEMENT OF RADIOTHERAPY TREATMENT INTERRUPTIONS

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Aim: Unplanned radiotherapy (RT) breaks lengthen the overall treatment time and have a negative effect on local control and cure rates. Here, we report the results of a recent nationwide study providing data on the main causes of radiation therapy interruptions and management strategies to reduce or eliminate their clinical impact.

Methods: Italian RT center directors participated in a study that investigated RT weekly schedules, the handling of RT interruptions, and guidelines use for handling interruptions.

Results: The survey was completed by 104 (56.8%) centers. With 2 (range 1-6) LINACS on average, only 5% of centers routinely conduct clinical activities six days a week; 22% of centers do so when dosage recovery is required; the remaining (73%) centers conduct clinical activities five days a week. The vast majority (93.1%) of centers considered interruptions a critical issue to manage, particularly for head and neck, cervix, lung and rectal cancer treatments. For 74% of respondents a 5-day or longer interruption could have an impact on the outcome of RT. The Royal College of Radiologists' international standards for interruption management were followed by 30 centers (28.88%), whereas 25 centers (24%) had their own set of rules. LINAC breakdowns (52%), toxicity (23%) and patient compliance (13%) were cited as the most frequent interruption causes. In the event of a LINAC breakdown, 80 centers have stated that patients will be treated in the other without recalculating the second machine. The majority of centers (86%) recover lost doses by raising the overall dose (79%), treating patients on Saturday (34%), holding two sessions per day (18%), using an accelerated regimen in the final part of the treatment (17%). Only 28 centers (27%) consistently recover dosage.

Conclusion: The nationwide survey revealed a variety of approaches to recovering from RT disruption, emphasizing the necessity of national rules and company advice.

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UNCONVENTIONAL FRACTIONATION SCHEMES WITH CONCOMITANT THERAPIES

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Radiation therapy (RT) represents one of the mainstays of cancer treatment. Despite the technological advances and remarkable improvements in dose conformation achieved in recent decades, normal tissue toxicity remains the primary factor limiting the efficient treatment of radioresistant tumors, lesions near radiosensitive structures (*e.g.*, spinal cord). Most of radiation is delivered in treatment fractions over days to weeks. The core aim of RT fractionation is the creation of a therapeutic window by leveraging differences in radiobiological principles between tumor and normal tissue. principles can be summarized by the "5Rs of Radiobiology", namely, Radiosensitivity, Repair, Reoxygenation, Redistribution, and Repopulation.

In many solid tumors, RT is combined with chemotherapeutic agents to improve treatment efficacy. This approach, is based on the premise that such combinations have spatial cooperation as the former targets the primary tumor site, whereas the latters target tumor cells outside the tumor irradiation field (micro- metastases).

Over the last decades, RT has been in the midst of new developments in technology. High-tech improvements have allowed for the maximal administration of dose to tumors while sparing normal tissues. In parallel, systemic therapies have been combined with radiation in an effort to improve tumor control. Conventional cytotoxic agents have improved survival in several tumor types but at the cost of increased toxicity due to effects on normal tissues. More recently, a better knowledge of the biological differences between tumor and normal cells as well as the differential responses of tumor and normal cells to radiation has prompted the investigation of molecularly targeted drugs and immunotherapeutic agents that may act synergistically with radiation. Only two targeted drug classes are considered standard therapy with radiation: epidermal growth fac- tor receptor (EGFR) inhibition with Cetuximab in head and neck cancer, and androgen receptor targeting with testosterone deprivation in intermediate and high-risk PC. This discrepancy can be in part explained by limited regulatory rules for drug-RT combination, as well as perceived challenges in designing trials with drugs developed specifically for use with RT, which should rely on relevant preclinical models. Definitely, the optimal dosing and timing

have to be explored.

Furthermore, predictive biomarkers are mandatory to drive treatment selection but only few have already been validated in patients receiving RT with molecular targeted therapy. In conclusion, the combination of modern RT and novel systemic compounds has the potential to translate in long-term clinical benefits for patients. A better understanding of new drugs and RT combination will require a truly multidisciplinary translational approach starting already in the preclinical phase and continuing through the clinical phase I, II, and III trials as well as during the post marketing studies.

5 FRACTIONS: THE NEW TREATMENT PARADIGM?

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During the past decade, there have been several innovations that have improved RT, including intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), and image-guided radiotherapy (IGRT). Thanks to this "hi-tech revolution", the reduction of the radiation treament sessions and the increase of dose per fraction have been progressively investigated. The use of hi-tech and ultrahypofrationation have represented the last frontier of this discipline by a technique called stereotactic body radiotherapy (SBRT) or more recently defined stereotactive ablative radiotherapy (SABR). In regard to this approach, the vast majority of data in prostate cancer was only available from limited series and phase 2 studies. Several mono-institutional reports have shown favorable toxicity and optimal 5-yr prostate-specific antigen (PSA) relapse-free survival outcomes for low- and intermediate-risk disease prescribing doses in the range of 35– 36.25 Gy in 5 sessions.[1-3] Follow-up at 5 and 10 yr showed that SBRT is well tolerated, with outcomes comparable with patients treated with conventionally fractionated intensity modulated radiation therapy (IMRT) . Regarding Prospective randomized trials, PACE B, randomly assigned 874 men (441 to convenctional RT and 433 to SBRT). 2-year RTOG toxicity rates were similar for five fraction SBRT and conventional schedules of radiotherapy. Prostate SBRT was found to be safe and associated with low rates of side-effects.[4] Several ongoing trials are exploring the concept of dose escalation with boost on the dominant lesion or the application of 5 session-SBRT schedules in High risk, trying to resolve the limits of pelvic irradiation. Another open discussion regards the concomiant use of androgen deprivation during 5 fraction-SBRT. Nevertheless, based on the available clinical evidence in the literature for low- and intermediate-risk patients, SBRT has recently become incorporated as part of treatment guidelines in regard to the management of localized prostate cancer.[5]

Regarding Breast cancer, after the randomized trial START a, START B, ONTARIO trial, the FAST FORWARD study has implemented ultrahypofractionation. More specifically: five-year local control after 26 or 27 Gy five fractions was non-inferior to 40 Gy 15 fractions. No evidence emerged that five-fraction regimens was inferior for any subgroup. 26 Gy five fractions side-effects, including subgroups, similar to 40 Gy 15 fractions. 26 Gy five fractions for breast radiotherapy, especially after covid, has been considered in some countries as the new standard of care.[6]

In rectal cancer, the Polish Colorectal Study Group showed that preoperative short-course radiotherapy followed by chemotherapy was comparable to chemoradiation in locally advanced rectal cancers. At 12 months' interval after intervention, the quality of life and ano-rectal and sexual functioning were not different in short-course radiotherapy group compared with those receiving chemoradiation.[7] The recently reported phase III randomized RAPIDO trial was ideated to compare these two schedules in patients with locally advanced rectal cancer. Overall survival at 3 years was equal, reported at 89.1% in the short-course therapy arm versus 88.8%. Morevover, there was no difference in the R0 resection rate in the short-course radiotherapy arm.[8] Thus, there is enough evidence that short-course approach in 5 sessions with full-dose chemotherapy given in the neoadjuvant setting can lead to preserved locoregional control, as well as distant disease control and pathologic response, without compromising the interventional intent and outcomes.

In conclusion, the oncology community, due to the emerging evidences and the COVID-19 pandemia, is rapidly rethinking hypofractionation implementation. It will reduce direct and inderect cost, waiting lists and could allow patients an immediate access to radiation therapy effective and safe cure worldwide.

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NEOADJUVANT CHEMOTHERAPY AND RADIOTHERAPY: WHAT'S THE EVIDENCE ABOUT RADIOTHERAPY VOLUMES AND DOSES?

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Neoadjuvant chemotherapy (NACT) has been widely adopted into the multidisciplinary management of breast cancer (BC). However, the impact of treatment response on the indication for adjuvant radiotherapy (RT) is unclear: while adjuvant RT is a well-established treatment modality in patients with BC, the evidence for the optimal use of adjuvant RT, target volume and doses after NACT is very limited. Different randomized prospective trials are ongoing, so, nowadays, available data came from retrospective studies. While it has been demonstrated that postmastectomy radiation therapy (PMRT) was beneficial for BC who are axillary lymph node-positive after NACT, the ALLIANCE A011202 trial[1] will gave answer about the RT fields (randomization: RT to level III + SVC + CMI in case of axillary dissection (levels I-II) vs RT to full axilla (I-II-III) + SVC + CMI if no AD). However, one of the most controversial questions regarding indication for adjuvant RT is whether or not RT is essential in patients with early stage disease at diagnosis with the value of adjuvant RT remaining highly debatable in those patients with clinically negative nodes at the completion of NACT.

The NSABP B-51/RTOG 1304 trial[2] is evaluating post-mastectomy/lumpectomy chest wall and regional nodal RT in patients with positive axillary nodes before NACT who convert to pathologically negative axillary nodes after NACT: this study will clarify the role of RT in this subset of patients with information about RT fields.

Another interesting ongoing trial is the RAPCHEM-NCT01279304[3] that stratifies both RT indication and field according to pathology findings Table 1.

All of the aforementioned studies administer RT according to conventional schemes; consequently, data about hypofractionation after NACT are scarse, but there is no reason to refuse moderate hypofractionation also for patients receiving NACT.

In conclusion, there is a considerable lack of evidence regarding the role of adjuvant RT and its individualization based on treatment response after NACT. Results of prospective randomized trials such as NSABP B-51/RTOG 1304, Alliance A11202 and RAPCHEM-NCT01279304 are eagerly awaited.

In the meanwhile, both RT indications, fields and dose fractionation should be personalized according to clinical stage, pathological response, tumor biology, number of removed nodes, and patient's preference.

Table 1. RAPCHEM- NCT01279304, stratification of radiotherapy according to pathology findings.

	Low risk patients	Intermediate risk patients	High risk patients
Axillary surgery and N stage	AD and ypN0 Or SNB	AD and ypN1 Or SNB	AD and ypN2 Or SNB
Prior CT characteristics	ypN1mi and no RF	N1mi with at least 1 RF or ≤2 N1mi with no RF	≤2 macrometastasis with RF or 3 positive nodes (macro/micro)
After CT characteristics	ypN0	ypN1mi and no RF	ypN1mi with at least 1 RF or ≤3 positive nodes (macro/micro)
RT FIELDS	MRM: NO RT BCS: RT to WB	MRM: RT to CW BCS: RT to WB If no AD, add RT to levels I-II	MRM: RT to CW + level III/SVC BCS: RT to WB + level III/SVC If no AD, add RT to levels I-II

AD: axillary dissection; SNB: sentinel nod biopsy; CT: chemotherapy; RF: risk factors; RT: radiotherapy; MRM: modified radical mastectomy; CW: chest wall; SVC: supraclavicular; BCS: breast conserving surgery; WB: whole breast.

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TOXICITY AND INTERACTION WITH SYSTEMIC AGENTS

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Radiotherapy (RT) is standard following neoadjuvant chemotherapy (NAC) and breast-conserving surgery. RT is used selectively following NAC and mastectomy: careful consideration of clinical stage at presentation, pathologic response to NAC, and other clinical characteristics, such as grade and biomarker status is required. The rate of pathological complete response (pCR) ranges from 13 to 22% among patients with human epidermal growth factor receptor 2 (HER2)–negative primary BC. After neoadjuvant standard therapy, further adjuvant therapy can now be individualized based on pCR status. In patients with pCR and with initially node positive BC should receive dual blockade for the remainder of the year. Extrapolation from the results of the adjuvant APHINITY trial suggest that continuing pertuzumab in the adjuvant setting is beneficial only in node-positive BC in terms of invasive disease–free survival (iDFS). In HER2-positive patients who did not achieve pCR following NAC, the postoperative treatment should be switched to antibody drug-conjugate trastuzumab emtansine (T-DM1), based on the results of the KATHERINE trial: iDFS was significantly higher in the T-DM1 group than in the trastuzumab group and distant

recurrence as the first invasive-disease event was lower in the T-DM1 group than in the trastuzumab group. Patients who do not have a pCR after the receipt of neoadjuvant taxane and anthracycline chemotherapy (CT) have a 20 to 30% risk of relapse. The CREATE-X trial found that the addition of adjuvant capecitabine was effective in prolonging DFS and overall survival (OS) among patients with HER2- negative BC who had residual invasive disease. The KEYNOTE-522 trial established that pembrolizumab in combination with NAC, followed by adjuvant pembrolizumab after surgery, for patients with stage II/III triple-negative BC (TNBC) was associated with a significant improvement in event-free survival over placebo plus CT. Among patients with high-risk, HER2-negative early BC and germline BRCA1 or BRCA2 pathogenic or likely pathogenic variants, adjuvant olaparib (a PARP inhibitor) after completion of local treatment and NAC or adjuvant CT was associated with significantly longer survival free of invasive or distant disease than was placebo, according to the OlympiA trial results. The monarchE trial found that combining the CDK4/6 inhibitor abemaciclib with endocrine therapy (ET) improved iDFS in patients with early high-risk HR+/HER2- BC. With the approval of these newer systemic treatments for BC and their expanding indications, it seems essential to understand whether these drugs can be safely and effectively paired with RT. It is necessary to continue to monitor side effect of association and develop new trials in order to better understand the interactions with RT.

GERIATRIC ASSESSMENT: FEASIBILITY AND IMPACT ON THERAPEUTIC CHOICES

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The geriatric Assessment consists of a set of tests and scores used to evaluate the elderly patient. In the oncological scenario, it focuses on the identification of the fragile and complex patient regardless of age, the quantification of patient resilience, and the Assessment of the risk of toxicity. Therefore, the primary purpose of its use is not the increase in survival but rather the reduction of toxicities, the risk of adverse events, complications, and the maintenance of the quality of life. It can quantify the risk of delirium or cognitive impairment in a patient undergoing CNS treatments through early identification of a chemobrain and a pre-treatment diagnosis of forms of cognitive impairment often not clinically recognized, such as MCI. It, therefore, falls directly within the scope of supportive care. The oncogeriatric Assessment, therefore, also has the function of a better definition of the patient, intending to carry out what can be defined as a "tailor-made" treatment, i.e., a treatment designed on the patient and concerning the patient's characteristics, overcoming the concept of personalization of therapies. The scores and tools should be chosen based on the reference setting (oncology/surgery/radiotherapy) and the neoplasm. They can be through screening (self-administered) or comprehensive Assessment. Respecting these characteristics, it is therefore not "time-consuming" but functional to the best therapeutic choice, maintaining a balance between overtreatment and undertreatment.

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HIGH GRADE GLIOMAS IN ELDERLY PEOPLE: THE ROLE OF RADIOTHERAPY

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The incidence of high grade gliomas (HGG) in the elderly population is slowly increasing in Western countries. Current management includes surgery, radiation therapy (RT) and chemotherapy; however, survival is significantly worse than that observed in younger patients and the optimal treatment in terms of efficacy and safety remains a matter of debate. Surgical resection is often employed as initial treatment for elderly patientsaffected by HGG, although the survival benefit is modest. Better survival has been reported in elderly patients treated with RT compared with those receiving supportive care alone, with similar survival outcome for patients undergoing standard RT (60 Gy over 6 weeks) and hypofractionated RT (25–40 Gy in 5–15 daily fractions). Temozolomide, an alkylating agent, may represent an effective and safe therapy in patients with promoter methylation of O^6-methylguanine-DNA-methyltransferase (*MGMT*) gene which is predictor of responsiveness to alkylating agents. An abbreviated course of RT, 40 Gy in 15 daily fractions in combination with adjuvant and concomitant temozolomide has emerged as an effective treatment for patients aged 65 years old or over with GBM. Results of the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG CE6) and European Organization for Research and

Treatment of Cancer (EORTC 26062/22061) randomized study of short-course RT with or without concurrent and adjuvant temozolomide have demonstrated a significant improvement in progression-free survival and overall survival for patients receiving RT and temozolomide over RT alone, without impairing either quality of life or functional status. Although combined chemoradiation has become the recommended treatment in fit elderly patients with GBM, several questions remain unanswered, including the survival impact of chemoradiation in patients with impaired neurological status, advanced age (>75–80 years old), or for those with severe comorbidities. In addition, the efficacy and safety of alternative therapeutic approaches according to the methyllation status of the O^6-methylguanine-DNA methyl-transferase (*MGMT*) gene promoter need to be explored in future trials.

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LE SFIDE FUTURE DELLA RADIOTERAPIA TRA INNOVAZIONE, CLINICA E SOSTENIBILITÀ MACCHINE IBRIDE

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Radiotherapy is currently indicated in up to 50% of cancer patients, both as exclusive therapeutic approach or as part of combined therapy workflows. Thanks to the recent technological advances, such as intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT) and stereotactic body radiotherapy (SBRT), it currently represents a safe and reliable treatment approach, allowing to deliver high dose levels to target volumes and able to ensure biological effectiveness, granting the respect of dose volume constraints for the surrounding organs at risk. The delivery of high radiation doses relies mainly on the possibility to verify patient's position and target volume location through image-guided radiotherapy (IGRT) solutions. The standard of care for IGRT is currently represented by on-board conebeam CT (CBCT) that allows to visualize soft tissues with acceptable resolution and anatomical detail. Nevertheless, the limited soft tissue contrast do not allow to take full advantage of IGRT principles, limiting dose escalation possibilities.

The recent introduction of Magnetic Resonance guided radiotherapy (MRgRT), that couples on board hybrid MR scanners with delivery units, has opened brand new perspectives for radiotherapy treatment optimization. On board MRI scanners allow indeed the direct visualization of both target volumes and surrounding organs at risk: this characteristic allows to identify therapy volumes that are generally poorly visualized on standard positioning imaging (i.e. duodenum). The real time imaging to track anatomical motion and gated delivery, is particularly advantageous for lesions under breathing movement influence (lung, upper abdomen). Detection of morphologic changes in anatomy of target and OaRs and their respective position allows planning adaptation on the actual shape and location, on a daily basis. These characteristics enables PTV margin reduction OaR sparing and ensures a safer delivery, paving the way towards more complete and comprehensive treatment personalization and adaptive solutions. In research, extraction, analysis, and comparison of radiomic features, are starting to promote dose-escalation response-adapted studies.

Despite the obvious advantages provided by this technology, the clinical role of MRgRT is still object of debate in the radiation oncology community, as the balance between the cost of these technologies and their real clinical impact is far from being demonstrated, while numerous pitfalls (i.e. MRI compatibility, claustrophobia, prolonged treatment times) still support skepticism about. Furthermore, the scarce number of active units and the existing technical differences among the available systems, do not allow to gather sufficient evidence and several studies are currently ongoing to better understand the potentialities of such an innovative technology, translating theoretical advantages into clinical and prognostic ones for the treated patients.

GO GREEN: TIME FOR GREEN RADIOTHERAPY WITH FOCUS ON PARTICLE BEAM TREATMENTS

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Aims: In the recent years the issues of climate changes and availability of resources are becoming essential and impact all areas of human activities. Numerous governments, international organisations, activists and scientists are hugely involved in the redefining and optimizing the human and societies' activities in order to guarantee its sustainability (ability to maintain or support a process over time). This applies to health care systems that becomes more and more complex and resource-dependent. In particular, oncology and radiation oncology have seen in the last decades an enormous development of technologies and new agents. The aim of this presentation is to review the available studies and trends in research regarding the sustainability of modern radiotherapy.

Methods: This is a narrative review of the literature and general trends in research regarding the sustainability

of modern radiotherapy with focus on particle beam treatments. The review concerned PubMed and internet domain (Google). The possible actions directed to the optimisation of resources are discussed.

Results: The PubMed review has shown no item for radiotherapy and ecology, however, some papers dedicated to radiotherapy and sustainability have been found.[1-4] The numerous actions have been found that lead to immediate or long-term reduction of resources allowing maintaining health care sustainable and available to larger papulation. These are some of the existing and potential actions:

1. Choosing wisely campaign – aiming in the resources optimisation (limitation of waste resources)
2. Hypofractionation
3. Telemedicine (telehealth)
4. Paper usage reduction (treatment charts, RT plans, Q&A documentations, instructions etc.)
5. Implementation of the strategies that aim in the improvement of therapeutic index (improvement of cure rate and/or reduction of acute and late toxicity) like particle beam treatments, FLASH, BNCT etc.
6. Development of personalised radiation oncology (new combinations, biomarkers including AI, radiomics etc.)
7. Innovation through energy saving new technologies
8. Evidence based use of radiotherapy as an alternative to more expensive treatments (for example, ablative radiotherapy instead of surgery, radiotherapy for oligoprogressive disease, palliative radiotherapy).

All these points regard particle beam treatments with particular attention to improved therapeutic index.

Conclusions: There is an increased interest in improving the sustainability of modern radiotherapy and oncology in general. Several existing actions and potential strategies have been identified. Wide adoption of these approaches can substantially increase the sustainability of cancer treatment and, considering the world wide scale of cancer, have an immediate impact of the world ecosystem.

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INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY)

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Aims: In the last years, we have observed significant progresses in interventional radiotherapy (IRT, brachytherapy, BT) technique, starting from imaging guidance implementation. Actually, several advancements have been observed in different phases of IRT workflow. The focus of this lecture is to detect emerging and developing technologies as well as future avenues of applications utilizing modern IRT.

Methods: An exhaustive narrative overview of the literature about innovation and new technologies in IRT has been explored.

Results: Image guidance has played a significant role in the improvement of IRT, leading to a more precise detection of target and delineation of normal tissues, resulting in a better tumor control as well as organs at risk (OARs) sparing, particularly in gynecological (GYN) and prostate cancer, but also in Head&Neck and skin management. In GYN field, MRI is the current imaging modality of choice for image-guided BT (IGBT) and standard guidelines for target delineation and contouring definitions are available, based on post implant CT or MR imaging. Several studies about intraprocedural imaging IRT interstitial catheter insertion, with the aim to obtain a better positioning of catheters in the tumor, are ongoing. As a consequence of imaging improvement, hybrid applicators CT-MR guided, combined intracavitary/interstitial applicators have been developed, in order to increase local control through dose escalation even for large and asymmetric tumors. In the same context, 3D printing process has begun to revolutionize IRT with a personalization of customizable applicators with complicated internal structures that can not be done with traditional IRT devices. This increasing implementation of IGBT and applicators has also led to a better definition of novel OARs, by facilitating their next inclusion in daily clinical practice with even more specific dose constraints. On the wave of radioimmunotherapy combinations, a few ongoing clinical trials are testing IRT with immune checkpoint inhibitors. In this setting, IRT appears to be a considerable partner of immunotherapy to enhance local tumor control and may systemize response in non-irradiated lesions. Lastly, the contribution of artificial intelligence can offer considerable benefits in the optimization of implant geometry, applicators location in treatment planning and source position in targets, avoiding OARs.

Conclusions: IRT has advanced significantly in the last decade due largely to improvements in imaging guid-

ance, applicators development and treatment planning. With the integration of IRT technique and advanced technologies, artificial intelligence and new systemic therapies, the future of IRT is even brighter.

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TECHNOLOGICAL BREAKTHROUGHS IN INTERVENTIONAL RADIOTHERAPY

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In the past recent years, we have seen an important technological breakthrough in the field of interventional radiotherapy (IRT, brachytherapy) that touched the "planning", the "delivery" and "catheters positioning techniques". These innovations, together with a multidisciplinary approach and the widespread use of 3D imaging techniques have led to the emergence of Image Guided Interventional Radiotherapy (or Image Guided BrachyTherapy, IGBT) resulting in an increase of treatment accuracy and therefore to major clinical and economic benefits in terms of increased local control and decreased toxicity. A significant contribution to this evolution has come from the industry through the development of sophisticated Remote After Loading machines (HDR and PDR), advanced treatment plan software and high-tech applicators that are increasingly smaller, easier to handle and MRI/CT compatible. The modern IRT indeed, offers the possibility of optimizing the coverage of the target by limiting the dose to organs at risk (Intensity Modulated Interventional Radiotherapy or Intensity Modulated BrachyTherapy, IMBT). The main advances in the field of "planning" have been determined by the introduction of systems of "image fusion", personalization of dose distribution, biological planning, automatic reconstruction of catheters and improvement in calculation of dose distribution also considering inhomogeneity. The preliminary results of the use of biological planning in brachytherapy are encouraging, although extensive validation is still required. Multicenter pooling of pre-treatment and treatment imaging and their correlation with clinical outcome data could contribute to build predictive treatment response models by creating supportive tools in order to improve catheter placement and treatment planning. The need to perform complex IGBT modalities has stimulated research in the radiobiological field for the identification of increasingly hypofractional therapeutic protocols. The last frontier of IRT is the introduction of Artificial Intelligence procedure.

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CAN EXTERNAL BEAM RADIOTHERAPY REPLACE INTERVENTIONAL RADIOTHERAPY?

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Brachytherapy, or Interventional radiotherapy (IRT), is an essential component of treatment for many types of cancers and it can be used alone or in association with external beam radiotherapy (EBRT) or surgery. The introduction of image guided IRT with CT or MRI based dosimetry and the development of new applicators permitting intracavitary and/or interstitial approach led to an increased oncological result in terms of local control and overall survival.

Some patients cannot be treated by IRT due to tumor dimensions and/or locations, anatomical variations, risk of bleeding, medical comorbidities that preclude anesthesia especially in the interstitial procedures, or patient's refusal due to due to anxiety or discomfort.

In addition, the availability of IRT in many facilities is relatively limited because it is highly operator dependent. During the last decades, the increased level of complexity in IRT procedures has led to the need of a dedicated team with a specific training, as it requires complex and advanced technical skills that, if absent, can significantly affect outcomes. In particular, the inadequate placement and/or displacement of the applicator could reduce both local control and disease-free survival rates.

Same analyses based on national and international databases such as the SEER (Surveillance Epidemiology and End Results), the NCDB (National Cancer Database) and the Quality Research in Radiation Therapy study have shown a gradually decreased use of IRT and in the same timeframe an increased use of IMRT and SBRT. The increasing disparity between National Health Service reimbursements for IRT compared with competing treatment modalities, such as IMRT and SBRT, has still more negatively affected the utilization of IRT.

Thanks to several technological progresses, new software for treatment planning and the evolutions of onboard imaging techniques, many EBRT departments were upgraded with the adoption of intensity-modulated radiotherapy (IMRT), volumetric arc radiotherapy, helical tomotherapy, stereotactic body radiotherapy (SBRT), and more recently with magnetic resonance imaging (MRI)-guided radiotherapy and proton therapy.

These sophisticated technologies allow for the sculpting of an IRT-like dose distribution with a rapid fall-off around the target volume, using hypofractionated large fraction doses. but two main issues need to be evaluated: target motion and progressive tumor shrinkage throughout the course of treatment. The real time tracking capability of modern EBRT allows to minimize the risk of a geographical miss and permits to reduce the CTV to PTV margin for intrafraction target motion. Multiple adaptive strategies have been implemented, including a personalized internal target volume, offline replanning and a plan of the day approach offering the possibility to modify the radiotherapy plan according to images acquired.

Different studies and systematic reviews have analyzed the experience in high-tech EBRT as an alternative to modern image guided endocavitary or interstitial IRT, in particular for locally advanced cervical cancer.

The preliminary experiences in EBRT for delivering a boost to the cervix were associated with worse overall survival and higher loco-regional failure rate than IRT, limited by old techniques delivering suboptimal doses, but in the more recent years, this gap is closing. Dosimetric analyses comparing EBRT and IRT shown different results according to the used techniques. Even though the dose distribution to the planning target volume were comparable, organ at risk exposure were higher in the EBRT groups, especially with IMRT alone. SBRT seems to be the most likely to replicate the IRT's dose gradient and inhomogeneous dose distribution, with a higher biologically equivalent dose and less PTV expansion compared with standard EBRT, leading to less volume of normal tissue irradiated.

SBRT was also evaluated as an alternative to IRT in the treatment of vaginal cuff in postoperative endometrial cancer, for accelerated partial breast irradiation, for skin cancer and for the treatment of localized prostate cancer either as a monotherapy or as a boost to EBRT.

In contrast to SBRT, thanks to the management of numerous subdivisions of beams, IMRT offers the possibility to develop the integrated boost concept with a high radiobiological impact in particular in the rapidly proliferating tumor where reduction of overall treatment time is beneficial. If IRT is supposed inadequate before starting EBRT, IMRT with simultaneous integrated boost (SIB) boost seems to be a promising technique. In cases when IRT is considered not applicable near the end of the EBRT, SBRT should be the preferred regimen.

During the last years proton therapy has become available for the treatment of different tumors. Thanks to distinctive physical characteristics, proton therapy offers dosimetric advantages compared to photon beam radiotherapy allowing a potential reduction of doses to organs at risk. Carbon-ion radiotherapy is also a promising treatment with a biological advantage due to its high linear energy transfer. Generally, a substantial reduction of the mean doses to organ at risk (e.g. femoral heads and bowel) and a low dose bath is obtained with proton in comparison with IMRT, even it is higher compared to IRT. Moreover, motion management systems still remains a difficult challenge. This is even more important in patients with cervical cancer, which are mainly young. Protons can reduce the dose to the normal tissue minimizing the risk of the stochastic effects of radiation.

A consensus treatment method for patients who are ineligible for IT has not been achieved to date. Although it cannot substitute IRT, modern EBRT boost (with or without implanted fiducial markers) can be a treatment

option for selected patients when IRT is not possible. Future clinical studies are required to test efficacy and safety of these techniques and to assess a useful organ at risk dose thresholds.

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Selected Oral Communications

B01

POSTOPERATIVE RADIOTHERAPY IN PN2 RESECTED NSCLC PATIENTS IN THE MODERN ERA: PRELIMINARY RESULTS OF A MULTICENTRE RETROSPECTIVE ANALYSIS OF ACUTE AND LATE TOXICITY (RAC-TAC STUDY)

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Background: Recently, LUNG-ART and J-PORT trial, both assessing the role of postoperative radiation therapy (PORT), have greatly changed the landscape of pN2 patients NSCLC patients undergoing surgery. In this scenario, the Italian Association of Radiotherapy and Oncology Lung Cancer study group has planned an observational multicenter trial aimed at evaluating toxicities of PORT in patients treated with modern techniques.

Methods: All acute and late toxicities (particularly cardiac, pulmonary and oesophageal) of PORT were retrospectively reported, analyzed and then related to clinical and dosimetric parameters. Collaterally, regional control, distant metastasis free survival and overall survival have been analyzed using Kaplan Meyer survival curves (significant when $p < 0,05$).

Results: Two hundred and twelve patients from 6 different centers have been included in the present analysis (142 males and 70 females, median age 68 years). One hundred-forty seven patients showed acute toxicity (69,3%), of whom 91 patients developed lung acute side effects (G1-G2 in 87 patients, G3 in 4 patients), 113 esophageal (G1-G2 in 112 patients, G3 in 1 patients) and finally only 4 cardiac (G1 in 2 and G3 in 2 patients). Sixty patients showed at least one late side effect (28,3%), mostly lung (43 patients G1-G2 and 1 G3) and esophageal (11

patients, all G1-G2); no late heart toxicity was reported. An history of heart disease was found to be significantly correlated with both pulmonary acute (p:0,016) and late toxicity (p:0,008). A correlation with dosimetric parameters was found between V30-Lung and late lung toxicity (p:0,007, cut-off V30-bil>15%) and between V5-Heart and acute cardiac one (p:0,043, cut-off V5>32%). With a median follow up of 54 months, 48 patients (22,6%) showed a locoregional relapse, while 106 patients (50%) developed distant metastases. Finally, 64 patients (30,2%) showed no evidence of disease and 55 patients (25,9%) were dead for disease. The number of positive nodes (p:0,015) was the only parameter correlated with distant metastases, while the total number of removed nodes (p:0,034) was related with locoregional relapse.

Conclusions: RAC-TAC retrospective study confirmed the low incidence of severe toxicities after PORT when delivered with more advanced technologies. At the same time, most of the patients develop distant metastases. The total number of removed nodes and the number of positive ones e significantly correlated with the pattern of recurrence.

B02

PRELIMINARY RESULTS FROM ARTO TRIAL (NCT03449719) A PAHSE II RANDOMIZED TRIAL TESTING ASSOCIATION BETWEEN ABIRATERONE ACETATE AND STEREOTACTIC BODY RADIATION THERAPY IN OLIGOMETASTATIC CASTRATE-RESISTANT PROSTATE CANCER PATIENTS

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Aims: ARTO (NCT03449719) is a multicentre, randomized phase II trial, testing the outcomes of association between Abiraterone Acetate (AA) and stereotactic body radiotherapy (SBRT) in patients affected by oligometastatic castrate resistant prostate cancer (CRPC). Here we present early results about biochemical response after 6 months from treatment start.

Methods: Oligometastatic CRPC (< 3 non-visceral metastatic lesions) were randomized 1:1 to receive either I line systemic treatment alone (abiraterone acetate, control arm) or association between systemic treatment and concomitant SBRT on all metastatic sites of disease (experimental arm). No previous therapy for metastatic CRPC were allowed. Both conventional staging and Methabolic imaging (e.g Choline or PSMA PET/CT) were permitted. SBRT should be administered providing at least a BED3 > 100. Complete biochemical response (CBR, defined as PSA < 0.2 ng/ml at 6 months after treatment) and biochemical response at 6 months after treatment start are the endpoints of the current analysis.

Results: One hundred fourteen patients were enrolled in ARTO trial, and included in the current analysis. Overall, 38.6% had a CBR (27.6 *vs* 50 % in the control vs experimental arm, respectively). After adjustement for baseline PSA, OR for CBR was significantly higher for patients undergoing SBRT, with OR 2.58 (95%CI 1.16-5.76, p-value 0.021. Moreover, linear regression model showed that patients in the experimental arm had a significantly lower PSA at 6 months (p=0.004).

Conclusion: SBRT showed to significantly improve biochemical response if compared to systemic treatment alone with Abiraterone Acetate in I line metastatic CRPC patients.

B03

DETECTION RATE OF 68GA-PSMA PET/CT FROM A PROSPECTIVE STUDY: PSICHE TRIAL (NCT05022914)

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Aims: PSICHE trial is a prospective observational study, exploring clinical outcomes after 68Ga-PSMA-11 PET/CT restaging at early biochemical relapse (BR) after radical prostatectomy (RP) +/- postoperative prostate bed radiotherapy. Here we present preliminary results focusing on 68Ga-PSMA-11 PET/CT detection rate and treatment provided on the basis of re-staging results.

Method: PSICHE (NCT05022914) is a prospective observational multicentric study including patients affected by BR after RP +/- postoperative prostate bed radiotherapy (BR defined as PSA > 0.2 ng/ml). All patients had a PSA at recurrence < 1 ng/ml. Patients undergo centralized staging with 68Ga-PSMA PET/CT and are managed according to a pre-defined treatment algorithm based on imaging results, including local and systemic therapy as indicated and outlined in the trial's protocol. Complete protocol details, including treatment algorithm, radiotherapy doses and fractionation allowed, are available on clinical trials.gov.

Results: Enrollment started on 19/03/2021 and is ongoing. Up to date, 92 patients have been enrolled. Median PSA triggering PSMA re-staging was 0.37 ng/ml (IQR 0.29-0.51). Overall, PSMA results were negative/positive in prostate bed in 69 patients (75%), while pelvic nodal or extrapelvic metastatic disease were detected in 18 (19.6%) and 5 (5.4%) patients, respectively. After re-staging, 20 patients (21.7%) underwent observation only due to previous postoperative RT (18) or patients refusal (2). Forty-eight (52.2%) patients were treated with prostate bed SRT, 18 (19.6%) underwent SBRT on pelvic nodal disease, 5 patients (5.4%) were treated with SBRT on extrapelvic oligometastatic disease. 1 patient who underwent ADT for PSMA detection of low burden metastatic disease. T-test showed no significant impact of PSA at recurrence or time to relapse on PSMA PET/CT detection rate (p=0.19 and p=0.09, respectively). ISUP grade < 3 was significantly associated with a negative PSMA PET/CT result (p=0.01), while D'amico risk cathegory (low/intermediate *vs* high) had no influence on PSMA detection rate (0.13).

Conclusions: 68Ga-PSMA PET/CT allowed a metastasis directed treatment strategy in 25% of population affected by oligometastatic extrapelvic disease, avoiding unnecessary ADT in 19.5% of patients already treated with postoperative RT. ISUP score resulted significant for PSMA detection rate, suggesting that risk of macroscopic relapse could be prominent in patients with baseline ISUP score 4 or higher.

B04

ATRIAL FIBRILLATION: WORLDWIDE PRELIMINARY DATA OF LINAC-BASED STAR PROSPECTIVE PHASE II TRIAL

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Purpose: In elderly, paroxysmal atrial fibrillation (AF) is difficult to treat with drugs and catheter ablation due to the higher complication rate. Thus, non-invasive approaches should be favorite. STereotactic Arrhythmia Radioablation (STAR) was used for ventricular tachycardia, but no data are available for LINear ACcelerator (LINAC)-based STAR in AF patients. Based on this background, the aim of present study was to determine whether LINAC-based STAR is considered safe for AF elderly patients.

Materials and Methods: The study was designed as a prospective phase-II trial started in May 2021, conducted in a single, referral center (ClinicalTrials.gov: NCT04575662). The inclusion criteria were: patients aged over 70 years, with symptomatic paroxysmal AF; intolerance or non-response to anti-arrhythmic (ATT) drugs. The primary study endpoint was the 1-month post-STAR safety, as complete STAR delivery and no acute treatment-related adverse events more than G3, assessed according to the Common Terminology Criteria for Adverse Events (version 5.0). Secondary endpoints were: reductions in AF episodes and in AAT, overall survival.

The sample size planning is 20 cases based on 95% success for the primary endpoint, with a significant level of 5% and a power of 90%. The date of the last follow-up was May 2022. All patients underwent to LINAC-STAR for a treatment dose of 25 Gy in 1 fraction to the area of the pulmonary veins.

Results: Here, the data of the first 16 worldwide patients treated were presented. All patients completed STAR, with an overall treatment time of 3 minutes. No acute treatment-related adverse events (≥G2) at 1-month from procedure were registered. At a median follow up time of 6 months (range 11-1), 4 patients (25%) developed acute G1 esophagitis, resolved with local lenitive oral treatment and 2 patients (12%) reported a mild asymptomatic pericarditis to the 6-months control chest CT. In 1 patient, cardiac arrest occurred 15 minutes after the procedure, requiring cardiopulmonary resuscitation, without subsequent sequelae. No late side effects, no AF episodes and no AAT use, were reported.

Conclusions: The LINAC-based STAR could represent a valid alternative for elderly excluded from catheter ablation.

B05

A PREDICTIVE MODEL OF POLYMETASTATIC DISEASE FROM A MULTICENTER LARGE RETROSPECTIVE DATABASE ON COLORECTAL LUNG OLIGOMETASTASES TREATED WITH STEREOTACTIC ABLATIVE RADIOTHERAPY: FINAL RESULTS FROM THE RED LAIT-SABR

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Aim: Stereotactic ablative radiotherapy (SABR) showed increasing survival in oligometastatic patients. Few studies actually depicted the oligometastatic disease (OMD) evolution after SABR. There are few evidences on which patient will remain disease-free and which will rapidly develop a polymetastatic disease (PMD) after SABR therefore apart from the number of active metastases, there are few data on what factor should be used for prescribing local treatment in OMD. The study aims to identify predictive factors of polymetastatic evolution in lung oligometastatic colorectal cancer (CRC) patients to tailor SABR prescription.

Methods: This international Ethical Committee approved trial (XXXXX) involved 23 Centers. The data of 450 lung oligometastatic patients were reported. Primary end-point was the time to the polymetastatic conversion (tPMC). Additionally, oligometastases number and cumulative GTV (cumGTV) were used as combined predictive factors of tPMC. Oligometastases number was stratified as 1, 2-3, and 4-5; cumGTV was dichotomized to 10 cc.

Results: The median tPMC in the overall population was 26 months. The median tPMC by oligometastases number was: 27.7, 21.3, and 9.4 months for patients with 1, 2-3, and 4-5 metastases, with a 2-year tPMC of 56.5%, 47.7%, and 39.2%, respectively (p=0.005). The median tPMC stratified for cumGTV was 33.1, and 13.5 months for cumGTV <10 cc or >10 cc, with a 2-year tPMC of 57.9%, and 37.5%, respectively (p=0.00). By combining these 2 factors we classified population in the following risk classes: low risk (1-3 oligometastases and cumGTV <10 cc) with a median tPMC of 35.1 months; intermediate risk (1-3 oligometastases and cumGTV >10 cc), with a median tPMC of 13.9 months, and high-risk (4-5 oligometastases, any cumGTV) with a median tPMC of 9.4 months (p=0.000).

Conclusion: the present study identified predictive factors of polymetastatic evolution after SABR in lung oligometastatic CRC. The results demonstrated that the sole metastases number is not enough to define the OMD since patients identified as oligometastatic from a numerical point of view might rapidly progress to PMD when the cumulative tumor volume is high. A tailored approach in SABR prescription should be pursued considering the expected disease evolution after SABR, with the aim to avoid unnecessary treatment and side effects in those at high risk of polymetastatic spread, and maximize local treatment in those with a favorable disease evolution.

B06

EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC UTERINE CANCER (MITO-RT2/RAD STUDY): A LARGE, MULTICENTER, RETROSPECTIVE STUDY IN COLLABORATION WITH MITO, AIRO GYN, AND MANGO GROUPS

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Objective: This retrospective, multicenter study analyzes the efficacy and safety of stereotactic body radiotherapy in a large cohort of patients with oligometastatic/persistent/recurrent uterine cancer.

Methods: A standardized data collection from several radiotherapy centres that treated patients by stereotactic body radiotherapy between March 2006 and October 2021 was set up. Clinical and stereotactic body radiotherapy parameters were collected. The objective response rate was defined as a composite of complete and partial response, while clinical benefit included objective response rate plus stable disease. Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer and Common Terminology Criteria for Adverse Events scales were used to grade toxicities. The primary endpoints were the rate of complete response to stereotactic body radiotherapy, and the 2-year actuarial local control rate on a 'per lesion' basis. The secondary endpoints were progression-free survival and overall survival, as well as toxicity.

Results: A total of 157 patients with oligometastatic/persistent/recurrent uterine cancer-bearing 272 lesions treated by stereotactic body radiotherapy at 14 different centers were selected for analysis. Of the sites of metastatic disease, lymph node metastases (137, 50.4%) were most common, followed by parenchyma lesions (135, 49.6%). The median total dose was 35 Gy (range 10-75.2), in five fractions (range 1-15). Complete and partial responses were found in 174 (63.4%), and 54 (19.8%), respectively. Stable disease was registered in 29(10.6%), while 15 (5.5%) lesions progressed. Patients achieving complete response on a 'per lesion' basis experienced a 2-year actuarial local control rate of 92.3% versus 29.4% in lesions not achieving complete response ($p<0.001$). The 2-year actuarial local control rate was comparable between nodal and parenchymal lesions. There were 43 acute toxicities reported, the most of which were minor (Grade 1 and Grade 2), and four of which were severe (two Grade 3 pain, one Grade 4 pain, and one toxic death due to gastric perforation).

Conclusion: Our analysis confirmed the efficacy of stereotactic body radiotherapy in oligometastatic/persistent/recurrent uterine cancer patients. The low toxicity profile and the high local control rate in complete responder patients encourage the wider use of stereotactic body radiotherapy in this setting.

B07

PROGNOSTIC VALUE OF INFLAMMATORY MARKERS IN LARC PATIENTS UNDERGOING NEOADJUVANT CHEMORADIOTHERAPY - PRELIMINARY RESULTS OF A LARGE RETROSPECTIVE MULTICENTRIC COHORT

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Aims: Patients (pts) affected by locally advanced rectal cancer (LARC) may respond differently to neoadjuvant chemoradiotherapy (nCRT). The identification of reliable biomarkers for oncologic outcomes could help in the development of risk-adapted treatment strategies. There is evidence of a role of inflammation parameters as prognostic factors for survival outcomes in different cancer types. Hemo-eosinophils inflammation (HEI) index, comprising systemic inflammation index (SII), hemoglobin (Hb) and eosinophils, was recently highlighted as predictor of disease-free survival (DFS) and overall survival (OS) in anal cancer pts. The aim of the present study is to evaluate baseline inflammatory markers as prognostic factors in a large multicentric cohort of LARC pts.

Methods: Pts undergoing nCRT for LARC from 2008 to 2019 were retrospectively analyzed. Pts underwent long-course RT with chemotherapy based on fluoropyrimidine ± oxaliplatin followed by delayed surgery; adjuvant chemotherapy was an option depending on risk factors. We collected data related to clinical and laboratory parameters, disease stage, treatments characteristics, pathological staging, and patients' status. Inflammatory markers were calculated on pre-treatment blood samples: HEI, SII, NLR (neutrophil/lymphocyte ratio), PLR (platelet/lymphocyte ratio) and MLR (monocyte/lymphocyte ratio). Their median value in the analyzed population was used as the cut-off value, except for HEI for which the cut-off was taken from the literature; Cox regression analyses were performed to study markers' correlation with our endpoints: OS, DFS, metastasis-free survival (MFS) and local control (LC).

Table 1. Inflammatory markers cut-offs and p-values for correlation with outcomes.

		Overall Survival			Disease Free Survival			Metastasis Free Survival			Local Control		
Marker	CUT-OFF	aHR	95%CI	p-value	aHR	95%CI	p-value	aHR	95%CI	p-value	aHR	95%CI	p-value
NLR	≥2.46	1.36	0.89-2.08	0.157	1.18	0.82-1.70	0.372	1.28	0.851-1.94	0.238	1.18	0.62-2.24	0.614
PLR	≥140.48	0.63	0.43-0.94	0.022	0.72	0.51-1.01	0.061	0.68	0.46-0.99	0.046	0.60	0.33-1.09	0.094
MLR	≥0.25	1.42	0.99-2.03	0.051	0.90	0.66-1.22	0.495	0.88	0.62-1.24	0.452	1.10	0.65-1.86	0.725
SII	≥603.1	0.99	0.60-1.64	0.987	1.13	0.72-1.76	0.594	1.18	0.71-1.95	0.523	1.32	0.60-2.92	0.486
HEI	≥2	1.18	0.78-1.79	0.429	1.02	0.71-1.47	0.900	1.08	0.71-1.63	0.728	0.77	0.40-1.46	0.422

Results: Overall, 1065 pts were eligible for analysis: 649 (60.9%) were males, median age was 64 years (range 27-91). RT was delivered with a median dose of 55 Gy (range 19.8-58.5). In our analysis [Table 1] we found a significant association between PLR and OS and MFS (HR=0.63 and 0.68 with p-value=0.022 and 0.046 respectively) where a PLR value higher than the cut-off (140.48) was related to a worse outcome.

Conclusions: These data suggest a possible correlation between baseline inflammatory parameters and oncological outcomes, in particular PLR, possibly related to host response to the tumor. A deeper insight into both systemic and local inflammatory markers could lead to the development of decision-making tools.

B08

SHARON BONE: FINAL RESULTS OF A PHASE III RANDOMIZED MULTICENTER TRIAL ON HYPOFRACTIONATED ACCELERATED PALLIATIVE RADIOTHERAPY IN BONE METASTASES

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Aims: SHARON BONE is a phase III randomized controlled multicenter trial aiming to demonstrate non-inferior symptoms relief, in painfully complicated bone metastases, of hypofractionated accelerated palliative radiotherapy (RT; 20 Gy in 4 fractions twice a day) versus a standard RT regimen (30 Gy in 10 daily fractions).

Methods: SHARON BONE involved 4 Italian RT units. Patients (pts) aged at least 18 years with ECOG PS < 3 candidates for palliative RT on painfully complicated bone metastases were eligible. We randomly allocated pts to either 30 Gy in 10 daily fractions (over two weeks), or 20 Gy in 4 fractions twice a day (in two consecutive days). Allocation was not masked because of the nature of the intervention. The primary endpoint was pain relief one month after treatment. Pain relief, toxicities, and Quality of Life questionnaires were also assessed at 2, 3, 6, and 12 months after RT. This trial is registered at clinicaltrials.gov (NCT03503682).

Results: Between February 2018 and December 2021, 83 pts were enrolled (30 Gy: 41; 20 Gy: 42). Pts characteristics are summarized in Table 1. Five patients on the standard RT schedule versus none in the experimental arm did not complete RT. Moreover, the primary endpoint was not evaluable in 5 pts (1 and 4 pts from the

standard and experimental arm, respectively) due to early death. Overall, the primary endpoint was evaluable for 73 pts (35 and 38 pts for standard and experimental arms respectively). Complete pain response (NRS=0) at 1 month was 22.9% and 28.9% in the 30 and 20 Gy arms, respectively (p: NS). The overall pain response rates (complete plus partial) were 82.9% and 86.8% in the 30 and 20 Gy arms, respectively (p: NS). Both treatments were well tolerated, with 12.2% and 4.8% pts experiencing G≥2 toxicity in standard and experimental arms, respectively. In the 30 Gy arm, two vertebral fractures were recorded.

Conclusions: 20 Gy in 4 fractions twice a day is non-inferior to the standard 30 Gy in 10 fractions for pain relief in complicated bone metastases, and it is at least as safe in terms of acute toxicity, with a lower rate of RT definitive interruptions.

Table 1. Patients characteristics.

		Number of patients (%)
Median age (range)	64 (23-88)	
Gender	Male	52 (62.7%)
	Female	31 (37.3%)
Primary tumor	Lung	19 (22.9%)
	Breast	14 (16.9%)
	Liver	9 (10.8%)
	Kidney	7 (4.8%)
	Prostate	6 (7.2%)
	Biliary tract	5 (6.0%)
	Other	23 (27.7%)
Metastases site	Spine	38 (45.8%)
	Pelvis	23 (27.7%)
	Rib and sternum	10 (12.0%)
	Scapula	4 (4.8%)
	Other	8 (9.6%)
Type of complication	Extraosseous extension	44 (53.0%)
	Nerve compression	18 (21.7%)
	Pathological fracture	11 (13.3%)
	Spinal compression	8 (9.6%)
	Not available	2 (2.4%)

B09

SALIVA MICROBIOTA AND INFLAMMATION MARKERS PREDICT ACUTE TOXICITY AFTER RT FOR HEAD-AND-NECK CANCER

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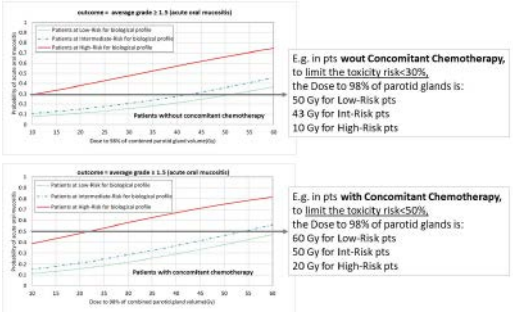
Aims: We hypothesised that saliva microbiota (MB) and cytokines levels differ between patients with/wout acute Radiotherapy (RT) toxicity for head&neck cancer (HNC).

Method: We enrolled 114 consecutive HNC patients (pts) treated with conventional (54-70Gy @2Gy/fr) or moderately hypofractionated (46.6-69.9Gy @2.1-2.2Gy/fr) VMAT+IGRT. A detailed evaluation was done pre-, during & at RT end, including saliva MB measures and cytokines assessment. Tox was scored weekly using CTCAE; average grade>1.5 for oral mucositis during RT (aOM), taking both severity & duration into account, was the endpoint for this analysis. We used logistic regression to derive cytokine signatures and unsupervised clustering to partition pts into MB clusters based on the relative abundance of Operational Taxonomic Units (OTUs) before RT start. Information on inflammation & MB clustering was introduced in a sigmoid-shaped dosimetric a Normal Tissue Complication Probability (NTCP) model to test their added value.

Figure 1. NTCP curves models including only clinical/dosimetric risk factors (dose to 98% to combined parotid glands, Oral Oncol 2018) and concomitant chemotherapy, and with the addition of biological information from saliva microbiota and IL6 concentration.



Results: Toxicity was scored in 22/114 pts. The baseline concentration of IL6 was significantly associated with acute tox: OR=1.8 (continuous log-scale, p=0.05). We defined a favourable IL6 profile if IL6 in the lowest 10° percentile (logIL6 (ng/ml) <0.7), 15.4 vs 36.8% aOM in favourable vs unfavourable IL6. MB clustered in 2 groups at the Genus level, with 9 genera included in the centroid signature. With Haemophilus, Neisseria, Prevotella and Streptococcus mostly driving the pts grouping. Pts in cluster B had a higher probability of aOM (unfavourable MB) compared to pts in cluster A (favourable MB): tox rates were 22.7 vs 14.6%, OR=1.7 (p=0.05). MB clustering was confirmed in the validation

cohort: tox rates 19 *vs* 32% in unfavourable vs favourable MB. To join information from MB and cytokines, we classified pts at low-risk (LR) of tox if they had "favourable MB AND IL6 profile", at intermediate-risk (IR) if "favourable MB OR IL6 profile", at high-risk (HR) if "unfavourable MB AND IL6 profile". Observed toxicity rates in LR/IR/HR were 12.5/16.7/41.2% (p=0.04). We obtained different tolerance doses for different risk classes when including "biological" stratification into a NTCP model (Figure 1).

Conclusions: We determined 3 risk classes for RT-induced acute side effects based on the combination of MB information and cytokine profile. The biologically personalised risk prediction improves discrimination and permits the design of possible interventional trials to reduce tox by modifying MB/inflammation levels before RT start.

B10

PREOPERATIVE ROBOTIC STEREOTACTIC RADIOTHERAPY IN EARLY BREAST CANCER: PHASE II ROCK TRIAL (NCT03520894)

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Aim: Breast-conserving surgery (BCS) followed by radiation therapy (RT) to the residual breast represents the current standard of care for most women affected by early breast cancer (BC). However, standard postoperative regimens are characterized by postsurgical waiting time and potential acute and late locoregional adverse events. Preoperative robotic stereotactic radiotherapy (SBRT) followed by BCS may yield potential advantages in selected patients. An exploratory phase II study was conducted in our institution.

Materials: Women with unifocal invasive hormonal receptors positive, HER2 negative BC, sized <25mm, with negative clinical nodal status, aged 50+ and eligible for BCS were enrolled. Fiducial markers were introduced in peri/intralesional position. Magnetic resonance imaging (MRI) was used in addition to standard CT-based planning. Patients received 21Gy in single fraction with CyberKnife followed by BCS 2 weeks after SBRT. The primary endpoint was the acute skin toxicity rate. Secondary objectives were the pathological response rate and the late adverse events rate. Echocardiography and spirometry were performed before preoperative SBRT and yearly thereafter. Translational research was conducted to identify correlations between radiogenomic, immunological and biochemical biomarkers with treatment-related response and toxicity.

Results: From August 2018 to September 2021, a total of 70 patients were screened on mammography; 29 of them were eligible. Seven were excluded due to multiple foci disease at basal MRI and 22 patients were successfully treated. All required dosimetric parameters and normal tissue constraints were met in all cases. Median age at diagnosis was 68 years (range 50-86) and median tumor size was 13 mm (range 7.5-25). All treated patients received BCS within 14 days from preoperative SBRT without any delay or complication. No patients experienced acute skin toxicity of grade (G) 2 or higher; only one patient had a G1 erythema one month after BCS. Two patients reported a pathological complete response, according to Chevallier's classification. At a median follow up of 18 months, no patients experienced locoregional recurrence or distant metastases. No clinically meaningful changes were observed regarding left-ventricular ejection fraction and spirometry.

Conclusions: The ROCK trial showed that single dose SBRT is a feasible technique in selected BC with a good safety profile and encouraging activity and warrants further investigations.

B11

RE-IRRADIATION OF INTRACRANIAL MENINGIOMAS FAILING AFTER PREVIOUS RADIATION THERAPY: AN ITALIAN MULTICENTER RETROSPECTIVE STUDY

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Aims: Re-irradiation (reRT) of intracranial meningiomas is often difficult due to the limited radiation tolerance

of the surrounding tissue. Aim of this analysis is to report outcome, toxicity and prognostic factors conditioning survival of re-irradiation of recurrent meningiomas (RM) with different radiotherapy modalities.

Method: We collected a multi-institutional database of meningioma patients who failing after radiation therapy and received reirradiation. Between 2003 and 2021, 185 patients (pts) were included. Patients were re-irradiated with different modalities: radiosurgery (SRS) (n = 79; 40.5%), multi-fraction stereotactic radiotherapy delivered in a median of 5 fractions (f-SRT) (n = 63; 34%), proton – therapy (PT) (n = 31; 17%) and conventional radiotherapy (n = 12; 8.5%). 110 pts were identified with WHO Grade I disease, 65 pts had grade II disease, and 10 pts had Grade III disease. Median age at re-irradiation was 62 years. Treatment planning was based on MRI with contrast and DOTATOC-PET. Biological equivalent doses in 2 Gy fractions (EQD2) for normal tissue and tumor were estimated for each course (a/b =2 for brain tissue and a/b = 4 for meningioma), as well as biological effective dose (BED). The primary outcome measure was progression-free survival (PFS). Secondary outcomes included overall survival (OS) and treatment-related toxicity.

Results: After a mean follow-up of 4.6 years (range 1.7-6.8) 3-year PFS is 51.6% and 3-year OS is 72.5%. At univariate Cox regression Ki67 >5% (HR 2.81, 95% CI 1.48-5.34, p=0.002) is negatively correlated with PFS while f-SRT (HR 0.32, 95% CI 0.19-0.55, p<0.001), longer time to reRT (HR 0.37, 95% CI 0.21-0.67, p=0.001) and higher tumor BED (HR 0.45 95% CI 0.27-0.76, p=0.003) are positively correlated with PFS. At multivariate Cox analysis only f-SRT, time to reRT and tumor BED maintained their statistically significant prognostic impact on PFS (HR 0.36, 95% CI 0.21-0.64, p<0.001; HR 0.38, 95% CI 0.20-0.72, p=0.003 and HR 0.47 95% CI 0.26-0.83, p=0.01 respectively). Concerning toxicity only larger tumor GTV has a statistically significant higher risk of acute and late toxicity (p=.0.004 and p=0.005 respectively). Radionecrosis occurred in 10% of the patients.

Conclusions: Reirradiation of RM progressing after previous RT appears to be feasible with promising clinical outcomes and an acceptable toxicity profile. Prognostic factors helping the physician in the decision making process have been identified and should be incorporated in daily practice.

B12

THE IMPACT OF HUMANITY ASSURANCE PROTOCOL (HAPPY) ON PSYCHOLOGICAL WELL-BEING IN GYNECOLOGICAL CANCER PATIENTS UNDERGOING INTERVENTIONAL RADIOTHERAPY

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Aims: Providing information in line with patients' needs is an important determinant for patient satisfaction and might also affect, distress, anxiety and depression levels of cancer survivors. Humanity Assurance Protocol in interventional radiotheraPY (brachytherapy)- HAPPY-defined the needs of patients undergoing interventional radiotherapy (IRT, also called brachytherapy) for gynecological cancer. This work evaluated as these series of recommendations/interventions may improve the psychological well-being of the patient during IRT.

Methods: Patients with gynecological cancer (endometrial and cervix cancer) undergoing IRT-HDR were analyzed. Patients filled three questionnaires during pre-IRT visit (T0) and at the end of IRT (T1): Distress Thermometer (DT, a self-reported international standardized tool using a 0-to-10 rating scale); a numerical rating scale for IRT procedure distress (NRS, where the patients indicate the intensity of the perceived pain assigning a number included between 0 to 10); Hospital Anxiety and Depression Scale (HADS, a well validated and reliable self-reported measure designed to identify the presence and severity of anxiety and depression in cancer patients).

Results: Fifty-five patients affected by gynecological cancer (42 endometrial, 13 cervix) and treated with high-dose-rate (HDR)-IRT were selected from January to May 2022. The median age was 64 (range, 35-84) years. According to the International Federation of Gynecology and Obstetrics the most of patients have Stage I for endometrial cancer (29/42) and for cervix cancer all patients presented locally advanced stage (IB-IVA). Most of patients have high education (51 patients, 92.7%) and are married or living with partner (38 patients, 69%). Only 14 patients (25.45%) are currently working. The HADS, DT and NRS average before IRT were 13.14, 4.58 and 5, respectively. The HADS, DT and NRS average after IRT were 12.31, 3.87 and 3.25, respectively. A Wilcoxon signed rank test analysis comparing T0 *vs* T1 scores

showed a significant improvement in DT (p=0.251), NRS (p< 0.00001) and HADS (p=0.034).

Conclusions: Interventional radiotherapy can be perceived as a stressful experience causing anxiety and distress for most women. Following clear interventions/recommendations, which are effective and inexpensive adjuncts, with the cooperation of an integrated, multidisciplinary team can 1) improve the emotional state of patients undergoing IRT and 2) be positive predictors for psychological outcome.

B13

MACHINE LEARNING BASED MODELS OF RADIOTHERAPY-INDUCED SKIN INDURATION FOR BREAST CANCER PATIENTS

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Fondazione IRCCS Istituto Nazionale dei Tumori; Fondazione IRCCS Istituto Nazionale dei Tumori; Fondazione IRCCS Istituto Nazionale dei Tumori; German Cancer Research Center (DKFZ); Montpellier Cancer Institute; Maastricht University Medical Center; Department of Oncology and Hemato-Oncology, University of Milan; University of Cambridge; Maastricht University Medical Center; Vall d'Hebron Institute of Oncology; University Hospitals Leuven; Universitätsmedizin Mannheim; Fondazione IRCCS Istituto Nazionale dei Tumori; University of Leicester; Icahn School of Medicine at Mount Sinai; University of Leicester; Fundación Pública Galega de Medicina Xenómica; Ghent University Hospital; University of Leicester; German Cancer Research Center (DKFZ); University of Manchester

Aim: To predict the risk of skin induration (SI) in breast cancer patients (pts) after radiotherapy (RT) using machine learning algorithm.

Methods: Pts were enrolled in 7 countries in Europe and US and treated with conventional/moderate or ultra hypo-fractionated RT with or without a tumour bed boost. Each centre followed local clinical practice, but the collection of data was standardised and centralised. Our endpoint was late grade 1+ (G1+) SI 2 years after RT. Inclusion criteria were: no SI at baseline and availability of complete data. Skin was defined as a 5-mm inner isotropic expansion from the outer body. To select a relevant portion of the skin DVH, we extracted the higher dose tail using different volume cutoffs (*i.e.* 25/50/etc cc volumes corresponding to 5x5-20x20cm^2 areas). We corrected sub-DHVs for fractionation using two a/b values 1.8 Gy, and 3.6 Gy. We calculated Equivalent Uniform Doses (EUDs) from corrected sub-DVHs, with n spanning from 1 to 0.05. We also considered the minimum dose (Dmin) of the selected DVH tail Toxicity models were built using feed-forward neural networks (10 neurons and 1 hidden layer) following a wrapper method for feature selection. We used separate datasets for input: clinical/treatment/genetic features were constant, while the dosimetric factors (EUDs and Dmin) coming from sub-DVHs varied with volume cutoff and a/b (Figure).

Results: The 647 pts included in the analysis had a G1+ SI rate at 2 years of 29.4%. 281 variables were considered: 127 published SNPs (GWAS literature), 40 clinical factors, 93 treatment factors and 21 dosimetric variables (for each volume and a/b). For volume thresholds <200cc, no dosimetric feature was selected by the wrapper method. Therefore, we derived a predictive model (16 features, no dosimetric variable) for use before RT planning (Model 1). At sub-DVH_200cc, for a/b=3.6Gy only Dmin was selected (Model 2) as dosimetric variable, while for a/b=1.8Gy, EUD (n=0.5) and Dmin entered the FNN (Model 3).

Figure 1 reports the selected features and performance of the 3 models.

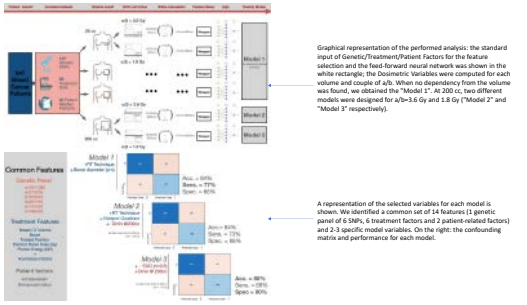

Figure 1.

Conclusions: A pre-planning SI model was derived that included information on genetics (6 SNPs), treatment (6 RT, 1 oncology) and clinical factors. Largest volume (200cc) sub-DVH allowed selection of dosimetric features, particularly with a/b=1.8Gy and EUD with n=0.5. Following validation, the model could be used to personalise use of new RT schedules, such as ultrahigh-hypofractionation, to minimise risk of SI.

B14

RADIOMICS IN DIFFUSION MRI FOR LOCALIZED PROSTATE CANCER CHARACTERIZATION (AIRC IG - 24946)

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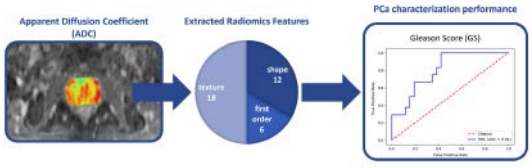
Aims: Prostate cancer (PCa) is the 2nd most common cancer in men. Several treatment options are available, making an accurate diagnostic and risk stratification essential to maximize the therapeutic benefits. Aim of this study is to investigate the potential of diffusion MRI-based radiomic models as a non-invasive tool for PCa characterization.

Method: Sixty-five patients with localized PCa, who underwent diffusion-weighted MRI (DWI) and enrolled for radiotherapy between 2014 and 2018 within the prospective AIRC IG-13218 trial, were included in the study. From mono-exponential fits of DWI, apparent diffusion coefficient (ADC) maps were estimated. Radiomic features (shape, first order, texture) were extracted from ADC maps of the whole prostate glands. After a feature-selection step involving one out of 5 selection routines (correlation, mutual information, Relief, RFECV, Mann-Whitney U-test), the best features were fed to different classification models (logistic regression (LR), support vector machine (SVM), random forest (RF)) investigating the ability to predict total Gleason Score (GS, 6 *vs* 7), risk class (NCCN, low *vs* intermediate), T-stage (T1 *vs* T2), extracapsular extension (ECE) score (2-3 *vs* 4), and Prostate Imaging Reporting and Data System (PI-RADS v2) score (2-3 *vs* 4-5) starting from ADC. Classification models were encapsulated in a 5-fold cross-validation routine. Receiver operating characteristic (ROC) curves were built, and the average precision (AP) was calculated for each score to access the accuracy of classification models. The predictive powers of the models built with radiomic features were finally compared, in terms of F1-score, with the ability of each clinical score to stratify patients according to GS.

Figure 1.



Results: From AP and ROC analyses, the best diagnostic performance was found for GS, reaching an AP of 0.78 and an area under the ROC curve (AUC) of 0.81 using RFECV as feature selection and LR as classifier (Figure 1). Among the 36 features with the highest predictive performance for GS, the textural ones were found to be the most frequent (12 shape, 6 first order, 18 texture). From F1-score analyses, the LR model was found to be the most powerful in predicting GS (F1=0.7) with respect to the conventional clinical scores (F1=0.42(ECE), 0.19(NCCN), 0.19(PI-RADS), 0.12(T-stage)).

Conclusions: Radiomic models based on DWI are a promising non-invasive tool for PCa characterization implying advantages for personalized therapy approaches.

AIRO GIOVANI
Oral Communications

C01

PLANNING STRATEGIES, MOTION MANAGEMENT, ACCURACY AND DELIVERY FOR STEREOTACTIC BODY RADIOTHERAPY IN PANCREATIC CANCER. AN UPDATE OF A NATIONAL SURVEY BY THE AIRO GASTROINTESTINAL STUDY GROUP

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Aims: Recently, notable technological advances in radiotherapy have significantly changed the management of pancreatic cancer. Stereotactic body radiotherapy (SBRT) resulted effective to delivery high dose/fraction to the tumor, but high quality of treatment is mandatory. In October 2018, the Italian Association of Radiation Oncology (AIRO) study group of gastrointestinal malignancies proposed a national survey to investigate the clinical practice of pancreatic SBRT. Aiming to assess how the Italian centers have adapted their procedures to new guidelines and evidence in this setting, an update of the

survey has been carried out.

Methods: The questionnaire was sent-back to all 22 Italian Institutions performing pancreatic SBRT and previously joined the survey.

Results: The 14% of the centers treats more than 20 cases/year and 32% ranged between 10 and 20 cases/year. Stereotactic body-frame is used in 6 centers (28.6%), whereas a frameless set-up is performed in most of the centers (71.4%). Organ motion control methods are used in the 81.8% (*vs* 63% in 2018) of the centers, (Figure 1a). The Simul CT with iodinated contrast medium is performed in 86.4% of the centers (vs 72% in 2018). Four centers performed MRI or PET-CT simulation. For Gross Tumor Volume (GTV) contouring, a rigid (45.45%) or dynamic (68.2%) co-registration is carried out. No preference of an imaging set is emerged but, a multiple approach is chosen (MDC TC: 64%, MRI: 68%, PET-CT: 64%). Clinical Target Volume is defined as GTV without margins in 7 (31.8%) centers. An individual Internal Target Volume is generated in 17 centers (77%). Intensity Modulated Arc Therapy (IMAT) is planned in 86.4% of the centers. A LINAC is employed in 77.3% of the centers (Figure 1b). Fiducial markers (2-3 in 50% of cases) are routinely placed for the target movement evaluation and/or a better localization in 27.3% of the centers (vs 19% in 2018). Image-Guided Radiotherapy (IGRT) is performed in all centers before each fraction. MRI LINAC-integrated and the 4D-CBCT are used in one center, respectively.

Conclusions: This survey illustrates the status of current technical strategies for pancreatic SBRT in Italy showing an improvement of high quality of treatment, as highlighted by modern systems for volume delineation, organ motion management (including fiducials placement) and delivery in almost all centers.

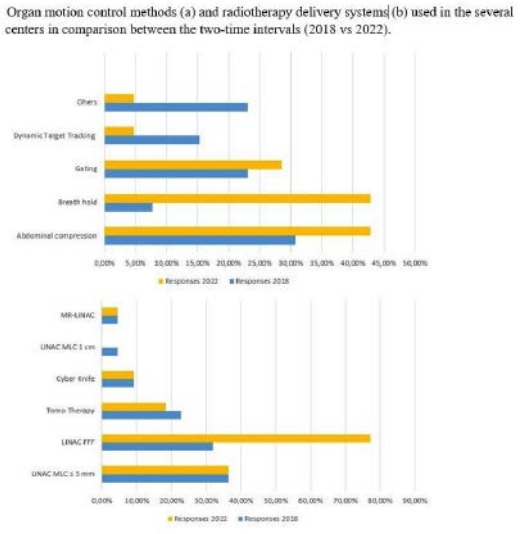

Figure 1.

C02

PATTERN OF FAILURE AFTER STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR OLIGOMETASTASES: PREDICTIVE FACTORS FOR POLI-PROGRESSION

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Aims: Patients with oligometastatic disease (OMD), defined as a maximum of 5 metastases in utmost 3 different organs, can be safely treated with Stereotactic Body Radiation Therapy (SBRT). Despite most patients relapse with oligometastases, some of them can experience a poli-progression after a local ablative treatment (LAT). The purpose of this study was to retrospectively identify predictive factors of poli-progression in patients receiving SBRT for OMD.

Method: Data from a monocentric database were retrospectively analysed. Patients treated with SBRT for OMD and who developed progression after LAT were selected. Patients were categorized as oligo or poli-progressive according to the number of new/progressing metastases (< or > 5). Herein, we analyzed data about patients' characteristics, oligometastatic presentation and radiation treatment characteristics to evaluate their relation with kind of progression. Univariate and multivariate Cox regression (backward conditional) model were used for this purpose.

Results: From 2013 to 2021, data from 1306 patients treated in our institution were collected. Of those, 700 progressing patients were retrospectively selected for this analysis. Baseline patients' and treatment characteristics are summed in Table 1. During follow up 227 patients (32,4%) experienced a poli-progression; median time to poli-progression was 7.72 months (range 1-79.6). Five variables predictive of poli-progression were found to be statistically significant at the univariate analysis: performance status ($p<0.001$), site of primary tumor ($p=0.016$), ablative dose ($p = 0.002$), treated site ($p=0.002$), single or double organ ($p=0.03$). Of those, four variables retained their significant predictive value on the multivariate analysis (Table 2).

Conclusions: Our study identified four predictive factors associated with poli-progression in patients with OMD receiving SBRT. According to literature, OMD patients may have various clinical presentations, heterogeneity about the course of disease and outcomes. Our data may support comprehensive characterization of OMD, better understanding of factors associated with progression and eventually improve the management of specific subgroups of patients.

Table 1. Baseline patients' and treatment characteristics.

Variables	Patients, No (%) (N=700)
Age (years)	
Mean	67
Median	74
Range	66-83
Sex	
Male	419 (59,9)
Female	281 (40,1)
Performance status	
0	422 (60,3)
≥1	278 (39,7)
Primary tumor site	
Colon	174 (24,9)
Lung	157 (22,4)
Breast	55 (7,9)
Prostate	60 (8,6)
Other	254 (36,2)
Primary tumor histology	
Adenocarcinoma	460 (65,7)
Squamous cell	47 (6,7)
Other	193 (27,6)
Metastatic presentation	
Synchronous	188 (26,8)
Metachronous	512 (73,2)
Disease-free interval (years)	
Range	0-18,2
Oligometastatic presentation	
De-novo	300 (42,8)
Repeat	102 (14,6)
Induced	298 (42,6)
Prior local ablative treatment	
Yes	255 (36,4)
No	445 (63,6)
Prior systemic therapy	
Yes	469 (67)
No	231 (33)
Previous systemic treatment lines	
1	294 (42)
2	111 (15,9)
>2	64 (9,1)
Number of metastases treated	
1	403 (57,6)
2	181 (25,9)
>2	116 (16,5)
Number of organs involved	
1	628 (89,7)
≥2	72 (10,3)

Variables	Patients, No (%) (N=700)
Irradiated lesions sites	
Lung	221 (31,6)
Brain	78 (11,1)
Liver	129 (18,4)
Adrenal gland	18 (2,6)
Lymph nodes	175 (25)
Others	79 (11,3)
BED (Gy)	
Median	100,2
Concomitant systemic therapy	
Yes	571 (81,6)
No	129 (12,4)

Table 2. Summary of multivariate Cox regression (backward conditional).

Predictor		p	Hazard Ratio
Ablative dose		0.01	1.54
Performance Status		<0.001	0.59
Treated site		0.003	
	Lung		0.31
	Brain		0.37
	Liver		0.58
	Adrenal glands		0.35
	Lymph-nodes		0.29
Primary tumor site		0.05	
	Colon		0.72
	Lung		0.86
	Breast		1.49
	Prostate		0.7

C03

STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH BONE OLIGOMETASTASES

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Aims: To assess the outcomes of oligometastatic patients treated with stereotactic body radiotherapy (SBRT) on bone lesions.

Methods: We retrospectively analyzed all the patients with bone metastases treated with SBRT at our center from February 2021 to July 2022. Eligible patients were aged over 18 years with oligometastatic/ oligoprogressive/ oligorecurrent disease from solid cancer, PS: 0-1, with symptomatic or asymptomatic lesions. Numeric rating scale (NRS) was used to assess pain value. Exclusion criteria were: severe disease that did not allow SBRT delivery. Target volumes were identified according to ISRC guidelines. SBRT was delivered by Helical Tomotherapy or Varian TrueBeam.

Results: The clinical data of 23 patients with 24 lesions undergoing SBRT were retrospectively evaluated. 19/23 (83%) were women and 4/23 (17%) were men. Median age was 65 (range 48-78). Three of 23 (13%) pts presented metastatic disease at diagnosis. 22/23 (96%) pts were oligometastatic on bones site and 1 patient on muscular and bone site (4%). At the clinical examination 10/23 (44%) were symptomatic with a median NRS of 5 (range: 2-9). The other 13/23 (56%) were asymptomatic. 10 pts (44%) were treated on spinal lesions and 13 pts (56%) on non- spinal metastases. In 6/23 (26%) pts, 5/23 (21%) and 1/23 (4%) SBRT target identification was guided by CT, PET/CT and MRI respectively, in the remaining 9 pts (39%) multiple diagnostic modalities were used. 16/23 (69%) received concomitant hormonal the-

rapy (HT) or Chemotherapy (CT). Median total dose was 40Gy (range:20-50), median dose per fraction was 10Gy (range:5-12) and median number of fractions were 5 (range:2-5). No severe toxicity (≥G3) were detected, 19/23 (83%) pts were asymptomatic at the end of the therapy, the other 4 pts (17%) presented mild symptoms like nausea, asthenia and pain flair. With a median follow up of 2.8 months (range:0.4-13.2), 16/23 (70%) pts demonstrated a radiological local control, the other 7/23 (30%) were in progression on the SBRT's target. 2/23 (9%) pts were deceased.

Conclusion: In our experience bone SBRT results feasible and safe; the majority of patients presented a complete remission of symptoms; we further evaluate QoL of these patients in a prospective study.

C04

STEREOTACTIC VENTRICULAR ARRHYTHMIA RADIOABLATION FOR VENTRICULAR TACHYCARDIA: SINGLE CENTER FIRST EXPERIENCE

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Aims: Stereotactic Ventricular Arrhythmia Radioablation (STAR) has emerged as a promising treatment option to precisely ablate the arrhythmogenic substrate of scar-related refractory ventricular tachycardia (rVT), in patients at prohibitive risk for catheter ablation (CA).

Methods: We present the experience with the first 2 patients treated with STAR for rVT at our Institution. The first patient treated was an 87-years-old man, hospitalised for rVT requiring ICD interventions, unresponsive to antiarrhythmic drugs. The second patient was a 60-years-old man, with rVT secondary to ischemic cardiomyopathy, presenting to the emergency department in VT storm requiring multiple ICD shocks and not responsive to maximal antiarrhythmic therapy. Both patients were considered not eligible for CA due to high intraprocedural risks. For target localization, high-density substrate electroanatomic cardiac mapping, cardiac computed tomography (CT) and magnetic resonance (MR) were acquired. To manage cardiac motion, a four-dimensional (4D) CT-simulation was adopted. Target volume definition was defined by Radiation Oncologists in cooperation with Electrophysiologists and dedicated Radiologists.

Results: STAR was delivered using 3 co-planar arcs configuration Volumetric Modulated Arc Therapy (VMAT). A photon energy of 6MV, flattening filter free (FFF) technique, and a dose rate of 1400 MU/min were used for both treatments. The prescribed dose was 25 Gy in single fraction to the Planning Target Volume, with a Dmax of 32 Gy to the arrhythmogenic substrate. To optimize image-guidance, a Cone Beam CT (CBCT) was performed before each arc delivery, and a respiratory-gated approach was used to monitor patients during fraction. The first patient was discharged from the hospital 1 week after STAR, while the second patient after 3 weeks. No acute or late toxicities related to STAR were reported. At 8 months and 4 months follow up for the first and second patients, respectively, no rVT were recorded during in hospital clinical evaluation and home monitoring ICD interrogation.

Conclusions: The present report confirms the efficacy and safety of STAR as a reasonable treatment option for patients with rVT not suitable for CA. Further investigations and longer follow up are needed to draw definitive conclusions.

C05

HOPE IS KINDLED: BI-WEEKLY HYPOFRACTIONATED RADIOTHERAPY IN ULTRA-ELDERLY WITH ADVANCED NON-MELANOMA SKIN CANCER

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Aims: In the COVID era, it is of paramount importance to achieve the optimal balance between the pandemic exposure risk and the chance to cure cancers. In this context, treatment of elderly patients with non-melanoma skin cancers (NMSC) is particularly challenging, especially for fragile patients (pts) unsuitable for surgery and/or with poor performance status (PF). NMSCs are radioresponsive and radiotherapy (RT) is a highly effective option with local control (LC) rates >95%. Usually, RT schedule consisted of 50-60 Gy (2-2.5 Gy/fx daily) over 4-5 weeks, but elderly pts with NMSC frequently have multiple morbidities such as pain and bleeding, thus daily treatment may be logistically difficult, considering also the pandemic. Hypofractionated RT delivered either daily, alternative daily or once/twice weekly is highly effective with tolerable toxicity and more pts' acceptability. Aim of the study is to evaluate safety and efficacy of a bi-weekly hypofractionated schedule in ultra-elderly pts with NMSC, in the pandemic era.

Methods: Between October 2021 and May 2022, 14 pts (10 male, 4 female), median age 89 years (86-98

years), with histologically proven NMSC were treated with exclusively hypofractionted bi-weekly RT. The histology was: squamous cell carcinoma (SCC) for 8 pts and basocellular carcinoma (BSC) for 6 pts. Median tumor size was 40 mm (range 35-63 mm), TNM staging was cT2 for 3 patients, cT3 for 11 patients, all pts (14/14) were cN0M0; RT prescription dose was 50-60 Gy in 10 fraction (5-6 Gy/fx bi-weekly) delivered with photon or electron. LC and toxicity profile (according to CTCAE v 5.0) were evaluated.

Results: Treatment was well tolerated, all pts completed RT without interruption. The median follow-up was 3 months (range 1-7 months). No pts had high grade (G3-4) acute toxicity; grade 2 acute skin toxicity was recorded in 2 pts (14%); grade 2 acute mucositis was recorded in 1 patient (7%). 9 patients (5 BSC and 4 SCC) had complete clinical and radiological response after a median of 5 months to the end of RT (64%); 6 pts had partial response, with a LC at 5 months of 100%. All the pts are alive. (Figure 1).

Conclusions: RT with bi-weekly schedule is a well-tolerated and safe treatment. This schedule allows to perform a curative treatment for ultra-elderly pts unfit for surgery or systemic therapy. Therefore, the bi-weekly schedule could be a good option for pts with poor PS and lead to a better compliance reducing the access in RT facilities.

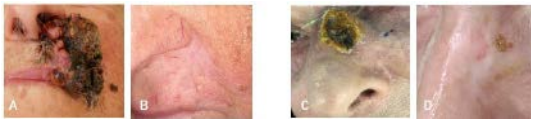

Figure 1. Examples of BSC (A) and SCC (C) treated with bi-weekly fractionated RT: Panel A/C: prior to RT: Panel B/D: 1-month follow-up.

C06

PSYCHOLOGIST'S KEY ROLE IN THE RADIOTHERAPY CARE PATHWAY: THE ROLE OF TELEMEDICINE

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Aim: During Covid-era, telemedicine has been increased also for phycological evaluation. The aim of this analysis was to investigate the role of psycho-oncologist during radiotherapy (RT) and the role of tele-consult.

Method: All patients during RT were welcome to receive freely and charge-free an assessment regarding their cognitive, emotional and physical state and related psycho-oncological support during treatment. A set of screening tests that investigate emotional distress and patient's mood is administered, including: Hospital Anxiety Depression Scale (HADS), Distress Thermometer, Brief Cope, Impact of Event Scale-Revised.

During RT, easy tools, such as Mindfulness-based stress reduction techniques, were performed to manage stress, reducing physical symptoms, mood and sleep disturbances. These psycho-therapeutic approaches were developed in individual sessions and/or in small group sessions. after RT, patients could be followed by tele-consultation or phycological evaluation on site.

Results: Between June 2019 and December 2021, 2727 patients underwent to RT. Of these, 2290 (84%) accepted to participate in psycho-oncological support program receiving at least a first evaluation. Excluding patients treated with short RT course (1-5 fractions), the remaining 1145 cases (50%) were followed during RT course with structured psycho-oncological interviews for a median of 3 sessions (range 2-5). In this subgroup, the median RT fractions were 25 (range 15-33). The median age was 60 years (range 20-78). Female were 1671 (73%) and male 619 (27%). Of the patients followed, 114 cases were followed for psychological disorders by external specialists. All patients completed their treatment without delay reporting a reduction in RT anxiety during the interviews and a "feeling of welcome". 82 patients were followed after RT, 30 with on-site consult and 52 with tele-consult. the consultation via web (video call) were well tolerated and comfortable for patients. However for phycologists, the evaluation of body is more difficult.

Conclusions: The role of phycologists after active treatment is necessary for some patients and the possibility of teleconsultation is helpful for patients but it is important for phycologist to improve his-her know-how for tele- evaluation.

C07

IMPACT OF COVID-19 PANDEMIC TO RADIOTHERAPY ACTIVITIES: A MONOINSTITUTIONAL EVALUATION

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Aims: In the 2020, COVID-19 pandemic had an indirect impact to all the hospital services, as well as oncological activities. This impact, especially in the early months of 2020, represented an issue for Radiotherapy Departments, often finding medical staff unprepared to face COVID-19 pandemic. Aim of this study was to assess the indirect impact of COVID-19 to all the activities in our Radiation Oncology Department.

Method: We retrospectively compared clinical activities trend in the following periods: January-December 2019, January-December 2020 and January-December 2021. Data related to clinical visits (first evaluations, follow-up), planning CT and PET/CT, treatment plannings and radiotherapy sessions on our 4 LINACs were examined.

Results: Results are reported in Table 1. In 2019 and 2020 the first clinical visits were respectively 2022 and 1890 recording an increase of 5.6% during 2021. Planning CT and PET/CT in 2020 were 1680, similar to 2019 (n=1675), instead in 2021 we recorded 1739 CT and PET/CT. The treatment plannings elaborated in 2020 were 1608 (vs 1585 in 2019, +1.45%) reaching 1643 in the 2021 (+2.2%). Follow-up visits rapidly decreased in March and April 2020, as shown in Figure 1, (n=1324 in 2020 vs 1757 in 2019, - 24.6 %), while in 2021 follow up visit were similar to pre-pandemic period (1660, +25.4%).

Table 1.

	First clinical visits	Planning CT and PET/TC	Treatment planning	Follow-up visits	Treatment sessions
2019	2022	1675	1585	1757	24341
2020	1890	1680	1608	1324	21880
2021	1996	1739	1643	1660	25402

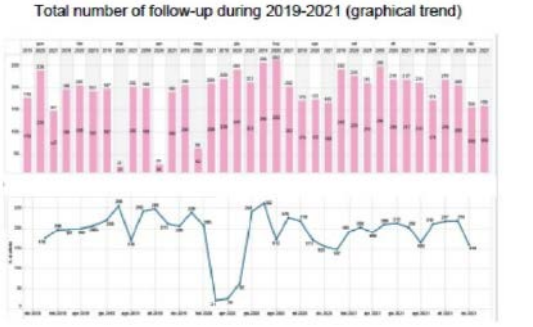

Figure 1.

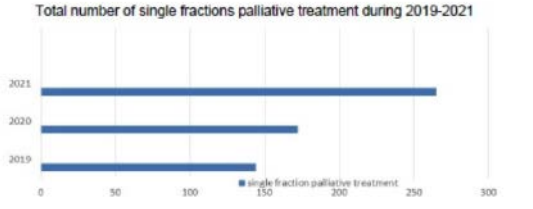

Figure 2.

During COVID-19 first (March, April 2020) and second (October, November 2020) peaks, follow-up visits were performed as tele-visits form in n=628; in the 2021 tele-visits were not performed. Total number of treatment sessions during 2020 was 21880 versus 24341 in 2019 (-10.1%), in 2021 treatment sessions registered an increase of 16.1% (25402). Hypofractioned regimens were preferred to reduce patients' treatment time (171 in 2020 vs 141 in 2019, with percent variations + 21.3%), this trend was confirmed in the 2021 for all pathologies, in particular single fraction palliative treatment reached +54% (267, Figure 2).

Conclusions: In the last 3 years, the activities of our radiotherapy department never stopped. Compared to 2019, our activity dropped mainly in the first months of 2020. This reduction regarded mostly patients' clinical visits, because of people fear of COVID-19 spread. During 2021, all activities increased progressively, the use of hypofractioned regimens were preferred for all pathologies.

C08

USE OF PERFUSIONAL PULMONARY SCINTIGRAPHY FOR THE EVALUATION OF RESPIRATORY FUNCTION IN PATIENTS DIAGNOSED WITH LUNG CANCER, ELIGIBLE FOR RT-CHT, IN THE COVID-19 ERA

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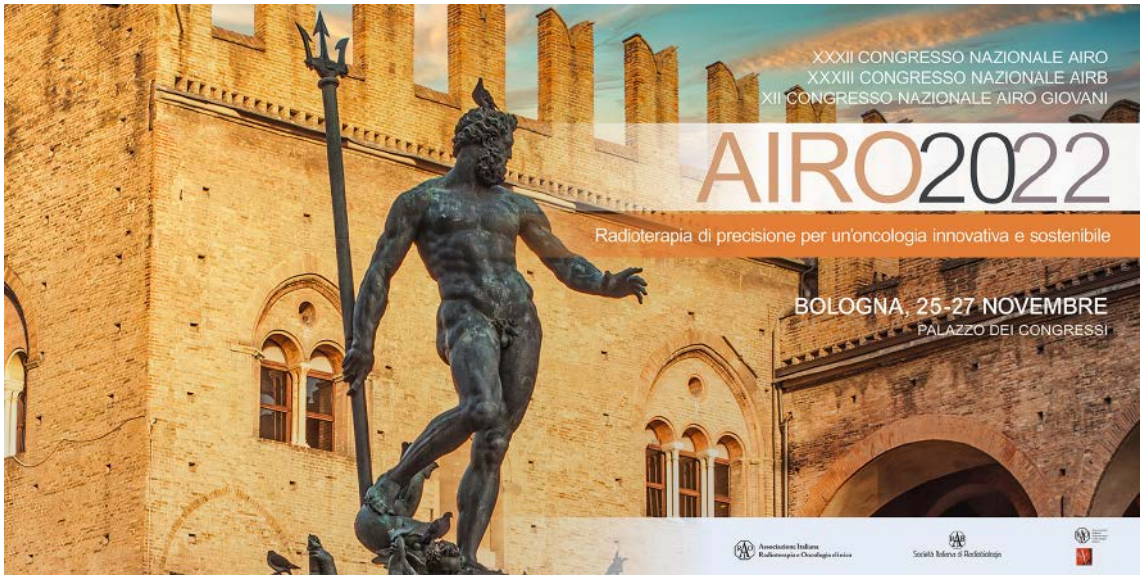
Aims: The spread of COVID-19 has made it necessary modifying the standard diagnostic protocols used. The drastic reduction or the complete impossibility to perform Spirometry and DLCO (most commonly used tests for the evaluation of respiratory function) has necessitated the obligatory replacement of this diagnostic standard with Perfusion Scintigraphy (only valid alternative). The reasons behind this circumstance was to decrease the chances of contagion (maximum by performing the spirometric examination, for both healthcare professionals and patients), even if this test involved higher health costs. mThis study evaluated the non-inferiority of Perfusional Pulmonary Scintigraphy (SPP) compared to Spirometry, for the evaluation of respiratory function and the consequent stratification of patients eligible for radiotherapy and chemotherapy treatment.

Methods: During the two-year COVID-19 emergency, patients diagnosed with lung cancer underwent SPP, for the stratification and their consequent classification in the correct diagnostic-therapeutic process. It was evaluated: the distribution of blood flow, its inhomogeneity, asymmetry, presence of hypoperfusion (global or localized in the individual pulmonary lobes), severe perfuse deficits. Post treatment CT scan chest was required and patients

were evaluated according to RECIST criteria.

Results: Between April 2021 and February 2022, 16 patients underwent SPP, of which 12 were males and 4 females. Median age was 70 years and different histological diagnoses (adenocarcinoma, squamous lung cancer or neuroendocrine cancer) and stages (from Ia2 to IVA) were identified. All patients underwent to radio-chemotherapy treatment (sequential or concomitant). Radiation treatment included: EBRT delivered in 14/16 patients, with median dose of 60 Gy (range 56-66 Gy) in 30 Fx (range 28-33 fx) (with Carboplatin AUC2+Paclitaxel for selected cases) and exclusive SBRT in 2/16 (total dose 50Gy in 5Fx or 45Gy in 3Fx). Post combination therapy CT scan evaluation demonstrated good clinical responses (SD or PR) in all the treated patients with no significant evidence of critical side effects.

Conclusions: Our results confirm the effective role of the SPP in the evaluation of the residual pulmonary function. SPP is a valid exam and a viable alternative that has to be considered for evaluation of the respiratory function in patients with lung cancer.



Oral Communications

CO01

RADIOTHERAPY IN PATIENTS RECEIVING ANTHRACYCLINES: PHASE 3 SAFE TRIAL (NCT2236806) INTERIM ANALYSIS

N. Bertini[1,2], I. Bonaparte[1,2], B. Bettazzi[1,2], C. Becherini[1], L. Visani[1], L. Marrazzo[3], I. Desideri[1], M. Casati[3], C. Arilli[3], S. Pallotta[4], L. Paoletti[5], S. Scoccianti[5], S. Russo[6], F. Martella[7], G. Simontacchi[1], V. Scotti[1], G. Francolini[1], M. Loi[1], M. Mangoni[1,2], C. Saieva[8], G. Barletta[9], I. Meattini[1,2], L. Livi[1,2]

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Aim: The SAFE trial is a four-arm, randomized, phase 3, double-blind, placebo-controlled study that evaluates cardioprotective strategies to prevent myocardial dysfunction. This is a subgroup analysis of the impact of postoperative breast radiation therapy (RT) on the first 174 patients who had completed cardiac assessment at 12-month.

Material: Patients with indication to primary or postoperative anthracycline-based chemotherapy were eligible. Cardioprotective therapy (bisoprolol, ramipril, or both drugs, as compared to placebo) was administered for 1 year from the initiation of chemotherapy or until the end of trastuzumab therapy. The primary endpoint was the detection of any subclinical impairment (worsening ≥10%) in myocardial function and deformation measured with standard and 3-dimensional (3D) echocardiography, left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS).

Results: At 12-month, 3D-LVEF worsened by 4.4% in placebo arm and 3.0%, 1.9%, 1.3% in ramipril, bisoprolol, ramipril plus bisoprolol arms, respectively (P = .005). GLS worsened by 6.0% in placebo arm and 1.5%, .6% in ramipril, and bisoprolol arms, respectively, whereas it was unchanged (.1% improvement) in ramipril plus bisoprolol arm (P <.001). Concerning differences in 3D-LVEF changes, bisoprolol-containing arms showed significant benefit in patients not receiving RT (P = .09), in patients receiving right-sided breast RT (P = .0001),

and with lesser extent, in patients receiving left-sided RT (P = .041). No significant benefit was shown in ramipril-containing arms. Concerning differences in GLS changes, bisoprolol-containing arms showed significant benefit in patients not receiving RT (P = .0001) and in patients receiving right-sided breast RT (P = .0001), while no benefit was shown in patients receiving left-sided breast RT (P = .270). Ramipril-containing arms showed significant benefit in patients not receiving RT (P = .035) and in patients receiving left-sided breast RT (P = 0.14), while no benefit was shown in right-sided breast RT (P = .260).

Conclusions: At the interim analysis, cardioprotective strategies in breast cancer patients receiving an anthracycline-based chemotherapy seem to protect against cancer therapy-related LVEF decline and heart remodeling. This favorable effect seems to be reduced in patients receiving postoperative left-sided breast RT, thus further investigations on potentially radiation-related early subclinical heart damage are needed.

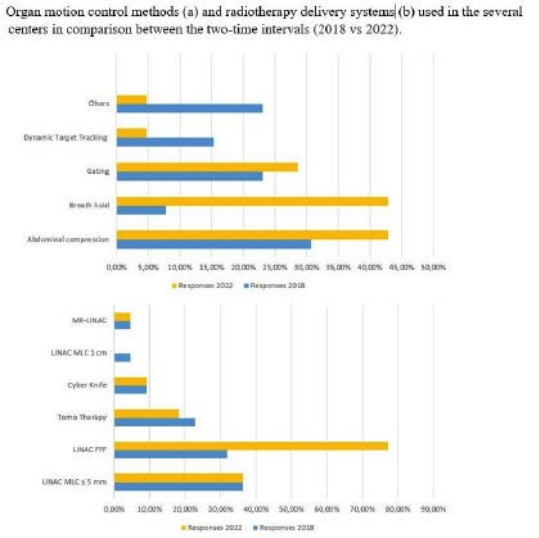

Figure 1.

CO02

SAFETY AND EFFICACY OF CDK4/6 INHIBITORS AND CONCOMITANT RADIATION THERAPY IN PATIENTS AFFECTED BY METASTATIC BREAST CANCER

B. Bettazzi[1,2], N. Bertini[1,2], I. Bonaparte[1,2], L. Visani[1], C. Becherini[1], E. Scoccimarro[1], V. Salvestrini[1], M. Valzano[1,2], I. Desideri[1], V. Scotti[1], C. Saieva[3], I. Meattini[1,2], L. Livi[1,2]

[1]Radiation Oncology Unit, Azienda Ospedaliera-Universitaria Careggi; [2]Department of Biomedical, Experimental and Clinical Sciences "Mario Serio", University of Florence; [3]Cancer Risk Factors and Lifestyle Epidemiology Unit, Institute for Cancer Research, Prevention and Clinical Network (ISPRO)

Aim: Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) currently represent the standard of care for the initial treatment of patients with metastatic hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) breast cancer. In this setting, a metastases-directed treatment with radiation therapy (RT) with either palliative or ablative intent is often required during systemic therapy. The aim of our study is to evaluate the safety and efficacy of the use of concomitant RT in a consecutive series of HR+/HER2- patients treated in two academic institutions with CDK4/6i in the metastatic setting, comparing with patients who did not received RT.

Materials: From September 2017 to February 2020, we retrospectively collected and analysed a sequential series of patients with metastatic disease treated with CDK4/6i, receiving RT or not, at two European institutions. Both hematologic and non-hematologic acute toxicity have been evaluated and scored according to CTCAE v5.0. Primary outcomes of the study were the impact of concomitant RT on any toxicity (any grade), any adverse events (AEs) equal or higher than grade 3 (≥G3), CDK4/6i dose reduction rate, and CDK4/6i treatment discontinuation rate.

Results: We analysed a total of 132 consecutive patients. The median age was 59 years (range 37- 86). RT was prescribed in 57 (43.2%) cases while 75 (56.8%) patients did not receive RT. Most patients were postmenopausal at the time of metastatic disease diagnosis (n=107; 81.1%). Seventy-three (55.3%) patients received letrozole and 59 (44.7%) fulvestrant as concomitant ET. Among patients who received RT, the majority was treated with palliative (n=44; 77.2%) versus radical intent (n=13; 22.8%). Concomitant RT administration was not significantly related to higher AEs ≥G3 (p=0.19) and any grade toxicity (p=1.0); there was no association with RT and CDK4/6i dose reductions (p=0.49) and discontinuations (p=0.14). At a median duration of follow-up of 18.8 months, the progression-free survival (PFS) rate was 65.0% and the overall survival (OS) rate was 38.7% in the whole group. The use of concomitant RT did not affect both PFS (p=0.71) and OS rates (p=0.55).

Conclusions: Our data are encouraging regarding the safety of this combination, showing that concurrent RT did not have an impact on systemic treatment conduction and did not increase toxicity.

CO03

STEREOTACTIC ABLATIVE BODY RADIOTHERAPY IN ELDERLY WOMEN WITH EARLY BREAST CANCER UNSUITABLE FOR SURGERY AND ELECTED TO RECEIVE PRIMARY ENDOCRINE THERAPY ALONE: PRELIMINARY RESULTS

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UOC Radioterapia Fondazione Policlinico TorVergata, Italy

Aims: To evaluate dose limiting toxicity (DLT) for Stereotactic Ablative Body Radiotherapy (SABR) for unresected breast cancer in elderly patients elected to receive primary hormone therapy alone.

Method: This is a prospective, single institution, open-label, phase I study of dose escalation SABR performed according to time-to-event Keyboard (TITE-Keyboard) design. We will enroll and treat 30 patients, in cohorts of size 10 patients, over 75 years, unfit for surgery or who decline surgery, with histologically confirmed diagnosis of early breast cancer (cT1-2 N0 M0), Luminal like A or B. Treatment dose levels will be 40Gy, 42.5Gy and 45Gy delivered with 5 fractions on every-other-day scheme. DLT, defined as any grade 3 or worse toxicity (per CTCAE v5.0), is assessed every 6 months. Patient reported quality of life (QoL) are evaluated using the combined EORTC QLC-C30 and QLQ-BR23 questionnaires at time zero, at the end of treatment, at 6 and 12 months, and then yearly. Cosmetic outcomes are evaluated through direct observation or indirectly through conventional photographs. Cosmesis evaluation are carried out before treatment, at last day of treatment and at every clinical examination with Harris scale scoring system and with Breast-Q v2.0 questionnaire.

Results: From February 2021 to May 2022 we have enrolled and treated 10 pts at first dose level of 40Gy/5fx with excellent tolerance to treatment. QoL questionnaires reported an improvement after treatment for 7/10 patients while all patients showed an excellent cosmesis. Five patients have at least 6 months follow-up after treatment and DLT was not reached. Four patients achieved a clinical and radiological partial response at 6 months, whereas 1 pt. showed a complete one's. In this small number of patients no differences were observed in the EORTC QLC-C30 and score and the breast cancer-specific score (QLQ-BR23) from the baseline at 6 months follow-up.

Conclusions: These are preliminary data on the first dose level in an ongoing phase I study, that will be updated at AIRO congress. In elderly patients eligible for hormone therapy only and unsuitable for surgery, SBRT could improve locoregional control by means of a short and highly effective treatment without any interruption of systemic treatment. The study is still enrolling patients at second dose level.

CO04

STEREOTACTIC BODY RADIOTHERAPY WITH CONCURRENT ANTI-CDK4/6 INHIBITORS FOR OLIGORECURRENT/OLIGOPROGRESSIVE BREAST CANCER PATIENTS

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Fondazione Policlinico Universitario Campus Bio-Medico di Roma, Italy

Aims: Stereotactic body radiotherapy (SBRT) for oligoprogressive/oligorecurrent metastases can delay next line systemic therapy. We evaluated safety and efficacy of concurrent SBRT with anti-CDK4/6 inhibitors in stage IV breast cancer patients.

Methods: The clinical records of metastatic breast cancer patients treated with SBRT to oligoprogressive/oligorecurrent lesions concurrently with anti-CDK4/6 inhibitors were reviewed. Toxicities were measured according to CTCAE 4.0. Response was evaluated according to RECIST/PERCIST criteria. PFS was evaluated from SBRT to local/systemic failure.

Results: Twenty-three patients treated to a total of 50 lesions were included in the analysis. Median age was 62 years (range 38-86 years). Mean Biological Effective Dose (BED) delivered (alpha/beta=4 Gy) was 89.3 (SD = 45). SBRT was delivered to bone metastases (58%), brain metastases (16%) and visceral metastases (26%). 10 patients were treated with concurrent Palbociclib (43.5%), 9 with concurrent Ribociclib (39.1%) and 4 with concurrent Abemaciclib (17.4%). Median FUP was 15 months (range 2-65 months). All lesions were evaluable for response: no patients experienced local failure on sites treated with SBRT. Response was evaluated on a per lesion basis. Complete response was achieved in 19 sites (38%), partial response in 17 sites (34%). After SBRT, 1-year and 3-year PFS were 16.8% and 30.5 % respectively. Mean duration of anti-CDK4/6 therapy after SBRT was 17.6 +/- 13.9 months. Only two toxicities were observed: a G1 dysphagia developed in a patient treated to a cervical spine lesion and a G3 neutropenia developed in a patient treated to a central lung lesion in 8 fractions.

Conclusions: SBRT for oligoprogressive/oligorecurrent breast cancer metastases delivered concurrently with anti-CDK4/6 inhibitors seems safe and effective and should be tested in prospective studies.

CO05

HALFMOON RADIOTHERAPY: A REAL-WORLD EXPERIENCE IN A SINGLE INSTITUTION

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[1]IEO European Institute of Oncology IRCCS; [2]Università degli Studi di Milano, Italy

Aim: The increasing use of immediate breast reconstruction (IBR) after mastectomy and its interaction with post-mastectomy radiotherapy (PMRT) has become a subject of great interest. In fact, besides the potential impact of RT on the cosmetic results, the reconstructed breast may affect the ideal target coverage and the optimal OARs sparing. Preliminary experience with implant-sparing RT using the HALFMOON (Helical ALtered Fractionation for iMplant partial OmissiON) technique and target contouring according to ESTRO-ACROP recommendation has been reported

Method: Breast cancer patients treated with mastectomy, either total or nipple sparing, and immediately reconstructed with implants (either tissue expander -TE or permanent implant-PI) and receiving Halfmoon RT by using TomoTherapy® Hi-Art System (Tomotherapy Inc., Madison, WI) in helical modality (TomoHelical) at the IEO between February 2020 and January 2021 were considered for the analysis. All the implants were placed beneath the pectoral muscle. As for our clinical practice, TE was fully inflated before RT. Contouring was based on ESTRO/ACROP guidelines for PMRT after implant-based IBR. The chest wall CTV is composed of ventral part (between the skin and the implant); in case of adverse tumor factors, the partial dorsal part (between the implant and the rib wall) is added to ventral CTV. Data about capsular contracture of the breast implant were collected according to the Baker classification.

Results: A total of 47 patients were analysed and their baseline characteristics are reported in Table 1. For patients reconstructed with TE, median time to TE substitution was 17.75 months. Considering patients with an IBR with PI only 1 patient out of 17 required implant substitution after 20 months. Toxicity assessment of capsular contracture, in a radiotherapy and/or plastic surgeon FU, was available for 34 out of 47 patients (72.3%) with a median follow-up (FU) of 1.2 years (IQR 1.0-1.7), Data about capsular contracture were available for 32/34 patients, with 28 of them reporting Baker grade ≥ 2, data were missing for 2 patients.

Conclusions: From the reported experience implant sparing RT using Halfmoon technique is technically feasible and preliminary data demonstrate an acceptable rate of capsular contracture. Data concerning additional toxicities and oncological outcomes are being retrieved.

Table 1. Summary of patients' characteristics.

Variable	levels	n (%)
age at surgery	49 years (IQR 44-54.5)	
T stage	*0*	3
	1	14
	2	22
	3	7
	x	1
N stage	*0*	9
	1	13
	2	13
	3	10
	x	2
Available FUs	*Radiotherapy*	25
	Oncology	9
	Senology	6
	Plastic surgery	28
	na	4
Type of reconstruction	*TE*	27
	PI	17
	na	3

CO06

OUTCOMES OF HYPOFRACTIONATED LOCOREGIONAL RADIOTHERAPY IN ADVANCED BREAST CANCER

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Aim: Hypofractionated radiotherapy (HRT) can be considered the standard treatment for breast cancer (BCa), but is generally applied for breast only RT. We report acute and late toxicity and outcomes in patients with advanced BCa treated with HRT to breast/chest wall (WBRT) and regional lymph-nodes (LN) in our Institute.

Methods: From 03/2018-03/2022 156 WBRT+LN HRT in 154 advanced BCa pts (2 bilateral, 98% female, 2% male) were performed in our Institute, after conservative surgery (56%) or mastectomy (42%), and as radical treatment in 3 pts (2%). Median age was 52 (26-86) years. Molecular subtypes were: Luminal A 31%, Luminal B Her2- 31%, Luminal B Her+ 16%, HR negative Her2+ 13% and Triple negative 9%. Neoadjuvant chemotherapy was prescribed in 52% of pts, adjuvant in 55%, and concomitant in 2.5%. Adjuvant hormonal therapy was prescribed in 77% of pts (IA or TMX -/+ LH-RH analogue), 31% of pts underwent HER2-targeted therapy. HRT was delivered with 3DCRT (10%), VMAT (30%) or Tomotherapy (60%), to a total dose of 40.05 Gy in 15

fractions, delivered in 3 weeks. A simultaneous integrated boost (SIB) up to 48 Gy to the tumor bed was delivered for pts with high-risk of local relapse (34.5%). The target was: WB+supra-clavicular (SCV) LN 35% (49% right, R, 51% left,L), WB+SCV+axillary LN 17% (44% R, 56% L), WB+SCV+axillary LN+internal mammary chain (CMI) 6% (44% R, 56% L), chest wall+SCV LN 29% (38% R, 62% L), chest wall+SCV+axillary LN 6% (22% R, 78% L), chest wall+SCV+axillary LN+CMI 7% (55% R, 45% L). Toxicity was registered according to CTCAE v 5.0.

Results: Median follow-up was 30 (7 – 68) months. No patient experienced ≥G3 acute toxicity. G2 skin toxicity was experienced in 16% of pts with SIB and 7.5% without SIB. Pts evaluable for late toxicity and outcome were 152. Acute and late toxicity is summarized in table 1. No significant differences in acute and late toxicity were found between the different RT techniques. Only one patient (metastatic at diagnosis and treated with radical WBRT+LN) had a local progression, 14 pts had distant progression. Eleven pts were dead at the last follow-up, 9 for systemic progression, 2 for other causes. Raw local control was 99.4%, DPFS was 90.8%, OS was 92.8%.

Conclusions: Locoregional HRT +/- SIB is feasible with low acute and late toxicity without significant differences in toxicities between the different RT techniques. Pts with SIB prescription who registered slightly higher toxicity, were treated with Tomotherapy.

Table 1. Acute toxicity in 156 WBRT+LN treatments and late toxicity in 154 treatments.

ACUTE TOXICITY	G0			G1			G2		
	3DCRT	VMAT	Tomo	3DCRT	VMAT	Tomo	3DCRT	VMAT	Tomo
Breast/chest wall erythema	13%	15%	14%	74%	72%	73%	13%	13%	13%
Axillary/supra-clavicular erythema	27%	28%	46%	67%	67%	48%	6%	5%	6%
Dysphagia	27%	33%	31.5%	67%	52%	55%	6%	15%	13.6%
LATE TOXICITY	G0			G1			G2		
	3DCRT	VMAT	Tomo	3DCRT	VMAT	Tomo	3DCRT	VMAT	Tomo
Hyperpigmentation	67%	57%	70.5%	0%	18%	22%	0%	0%	2%
Edema	67%	57%	70.5%	33%	25%	7%	0%	4.5%	2%
Fibrosis	93%	79.5%	88%	0%	11%	5%	0%	0%	0%
Pain	93%	79.5%	88%	7%	9%	3%	0%	0%	1%
Telangiectasia	93%	79.5%	88%	0%	0%	1%	0%	0%	1%

CO07

RADIOTHERAPY (RT) IN OLIGOPROGRESSIVE METASTATIC BREAST CANCER (MBC)

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Aims: With the introduction of new target therapy and the improving of imaging, oligoprogressive disease is even more common in the clinical practice. In these setting, RT in all sites of disease progression could represent a valid treatment to improve disease control maintaining the same systemic treatment (ST). Aim of this update to our series is to evaluate the outcome of pts receiving RT for oligoprogressive mBC.

Methods: A retrospective analysis including mBC patients (pts) undergone RT on up to three sites of oligoprogression with prosecution of systemic therapy was conducted between January 2014 and January 2022. Primary endpoints was progression-free-survival after radiotherapy (PFS-AR). Rate of disease progression at first assessment after radiotherapy (RDP-AR) and overall survival (OS) were secondary endpoint. Subgroup analysis (age, immunophenotype, line of therapy, site of oligoprogression) was performed. Multivariate analysis was performed to predict PFS-AR.

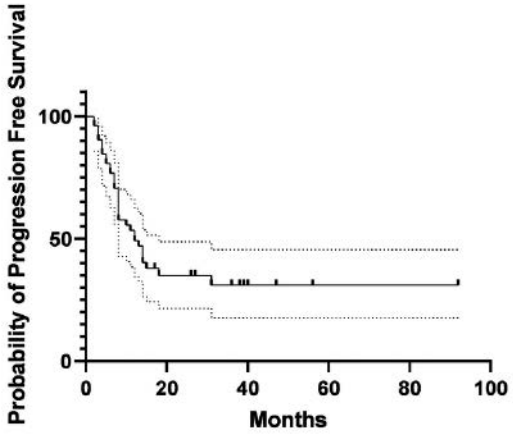

Figure 1.

Results: On 954 mBC who underwent radiotherapy, 52 pts met inclusion criteria. The median follow-up was 29.7 months (m). PFR-AR was 12.7 m (95% CI 8.5-18.8 m). RDP-AR was 15,3%. PFS-AR was not significantly

different between immunophenotypes with a median PFS 11.6, 13.9 and not reached, respectively for luminal-like (25 pts), HER2+ (23 pts) and triple negative (4 pts). Pts with ongoing up to second line of ST significantly presented a better PFS-AR, in comparison with pts with further lines: 14.1 vs 7.3 months (HR: 0.3, 95% CI 0.1-0.94, p=0.009). At multivariate analysis conducted for PFS-AR line of therapy maintained an independent prognostic value (p=0.013). OS was 84 months (95% CI 52,5-84 months).

Conclusions: Pts with oligoprogressive metastatic breast cancer treated with radiotherapy to all progressive sites seems achieve long-term progression-free survival, especially during first two line of systemic therapies. Data from prospective and larger population trial are necessary to confirm this data.

CO08

BREAST RE-IRRADIATION AFTER SECOND CONSERVATIVE SURGERY IN PATIENTS WITH IPSILATERAL BREAST CANCER RECURRENCE: MULTICENTRIC OBSERVATIONAL RETROSPECTIVE STUDY

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Aims: Salvage mastectomy has historically been considered the gold standard treatment for patients with breast recurrence after conservative treatment, although no phase III studies are available comparing these two therapeutic approaches. This Italian multicentre observational retrospective study was designed in order to evaluate the different breast re-irradiation techniques available on the national territory as an alternative to rescue mastectomy and to summarize the respective oncological, toxicity and cosmetic outcomes.

Method: A data base was performed in order to collect data on patients selection criteria, tumor biology, time interval between primary tumor and relapse, treatment technique, irradiated volumes, fractionation schedule, acute and late toxicity profile, assessed using the CTCAE v.5 scale. Quality of life according to the QLQ-C30 scale and cosmetics according to the HARVARD-Modified Cosmesis Grading Score. Inclusion criteria: age ≥ 18 years; infiltrating and in situ breast cancer, subjected to retreatment after second conservative surgery, written informed consent. Exclusion criteria: patients undergoing mastectomy, inoperable patients, absence of informed consent to the processing of data for research purposes.

Results: A core group made up of 4 Italian radiotherapy centers evaluated the feasibility of the database and collected data from 46 patients suffering from ipsilateral breast recurrence, all of whom underwent a second conservative surgery and subsequent reirradiation during the previous three years (2019-2021). There was complete agreement on the data to be collected. The majority of the patients underwent partial irradiation (38/46). The external beam techniques used were 3DCRT, tomotherapy, VMAT. No grade 3/4 toxicities were reported.

Conclusions: Reirradiation after second conservative surgery seems to be a feasible alternative to salvage mastectomy in selected patients with ipsilateral breast tumor recurrence. Partial breast re-irradiation seems to be the preferable option. A longer follow-up is needed in order to analyze the late toxicity and cosmetic data.

CO09

ROLE OF RADIOTHERAPY IN LARYNGEAL CANCER UNDERGOING PARTIAL SURGERY: PRELIMINARY ANALYSIS OF A MULTICENTER STUDY

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Aims: Laryngeal cancer treatment approach depends on AJCC stage, providing a single modality approach, surgery or radiotherapy for early stage, while a multimodality approach in locally advanced stage. With the aim of preservation of laryngeal functions, partial laryngectomy (partial horizontal laryngectomy (OPHL) or transoral laser microsurgery (TLM)) could be proposed in selected patients followed by postoperative radiotherapy (PORT) when recommended according to guidelines. Anyway, in pathological intermediate stage the indication to PORT after partial surgery is controversial due to poor literature's evidence. We aimed to analyze the oncological outcomes in patients who underwent partial OPHL or TLM, with or without PORT.

Table 1. Main characteristics of patients.

Characteristics	Category	Prevalence Number (%)
Sex	Male	246 (87.85)
	Female	34 (12.15)
Grading	G1	11 (3.9)
	G2	175 (62.5)
	G3	87 (31.1)
	Unknown	7 (2.5)
pT stage	T1	4 (1.4)
	T1a	1 (0.35)
	T1b	4 (1.4)
	T2	104 (37.1)
	T3	129 (46,1)
	T4a	38 (13.6)
N stage	cN0 or pN0	201 (71.7)
	pN1	35 (12.5)
	pN2a	2 (0.7)
	pN2b	20 (7.1)
	pN2c	12 (4.2)
	pN3b	10 (3.5)
Surgical Margins	R0	166 (59.3)
	R close	38 (13.6)
	R1	76 (27.1)
LVI	Positive	82 (29.3)
	Negative	148 (52.7)
	Not specified	59 (21)
PNI	Positive	82 (29.3)
	Negative	139 (49.7)
	Not specified	59 (21)
Subsite	Glottic	62 (22.1)
	Sovraglottic	82 (29.3)
	Not specified	136 (48.6)
Surgical technique	TLM	118 (42.1)
	OPHL	159 (56.8)
	Not specified	4 (1.5)
Adjuvant Radiotherapy	Yes	116 (41.4)
	No	164 (58.6)
PORT pT2	Yes	29(27.8%)
	No	75(72.2%)
PORT pT3	Yes	56(43.4%)
	No	73(56.6%)
PORT pT4a	Yes	25(65.7%)
	No	13(34.3%)
PORT pN0	Yes	29(33.7%)
	No	57(66.3%)
PORT pN1	Yes	21(60%)
	No	14 (40%)
PORT pN2a	Yes	2(100%)
	No	0
PORT pN2b	Yes	16 (80%)
	No	4 (20%)
PORT pN2c	Yes	10 (83%)
	No	2 (17%)
PORT pN3b	Yes	9(90%)
	No	1 (10%)

Method: A retrospective analysis was conducted in two Centers: inclusion criteria consist of histologically diagnosed squamous cell laryngeal cancer subjected to TLM or OPHL followed by PORT or not, mainly pT3-T4 pN0 and pT1-T3 pN1 (called here "intermediate").

Results: From 2005 to 2022, 280 patients were included in the analysis. Main characteristics of patients are showed in Table 1. TLM or OPHL were performed in 118 and 159 patients respectively. Patients were mainly pT2 (37.1%) and pT3 (46.1%) and pN0 (71.7%) or pN1 (12.5%). PORT was administered in 116 patients (41,4%). With a median FUP of 39 months (range, 2-97 mo), a recurrence of disease was observed in 24,7% of patients with a median time to relapse of 19 months. A significative difference ($p < .05$) in loco-regional relapse was observed between patients who received PORT or not, respectively in 18/116 (18%) and 51/162 of cases (31.4%). DFS at 5 years was 78% in patients who received PORT and 63% in the no RT group ($p < .05$) and the beneficial remains in the subgroups analysis for "intermediate" stage. Overall survival (OS) in patients who received PORT or not, was 88% and 95% at 5 years and 54% and 40% at 10 years, respectively ($p < .03$).

Conclusions: According to literature's evidence, PORT is mainly indicated in more advanced stage where it has been proved that impact on DFS and OS. Our results confirm the role of RT, also in patients addressed to partial surgery for laryngeal carcinoma and pathological "intermediate" characteristics. Prospective studies are needed to further confirm these results.

CO10

IS IT TIME TO SPARE POSTOPERATIVE IRRADIATION OF THE FLAP IN LOCALLY ADVANCED ORAL CAVITY TUMOURS TREATED WITH COMPARTMENTAL TONGUE SURGERY AND RECONSTRUCTION? RETROSPECTIVE ANALYSIS OF 183 PATIENTS

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Introduction: Surgical flap is routinely included in target volumes of postoperative radiotherapy (PORT) in patients treated with surgery for locally advanced tumor of the oral cavity. Due to its volume and location, irradiation of the surgical flap could increase the acute radiation-related toxicity. We performed a retrospective analysis on consecutive patients treated with compartmental tongue surgery (CTS) and subsequent PORT in two Italian Institutes aiming to assess whether the surgical flap represents a site of tumor local recurrence.

Method: Data from patients with oral cavity carcinoma treated with CTS and PORT at two Italian Institutes have been retrospectively collected and analyzed. Inclusion criteria were: 1) locally advanced stage (III and IV according 7th AJCC staging system), 2) CTS, 3) PORT and 4) minimum follow-up of 6 months. Localization of local recurrences has been identified both by radiologic images (if available) and by the revision of

medical charts performed by an expert surgeon (RB). All patients have been treated with intensity modulated radiotherapy (IMRT) up to a total dose ranging from 54 to 66 Gy. The surgical flap was always included in the RT treatment field at different dose levels according to tumor characteristics.

Results: One hundred and eighty-three patients matched the inclusion criteria. Clinical and pathological data have been summarized in Table 1. For the whole cohort, median age was 54 years (IQR: 45 – 64 years). Glossectomy of type III, IV, V and VI was performed in 95 (52%), 39 (21%), 8(4%) e 41 (23%) pts, respectively. After a median follow-up time of 74.1 months (IQR: 29.1 – 120.4), 52 pts were alive without evidence of disease. Twenty-eight pts died for tumor progression. Twenty-eight (15%) pts experienced a local recurrence after a median time of 9.4 months (IQR: 7.8 – 20.5). Among them, local recurrence was identified through radiologic images for 17 pts and through clinical charts revision for 11 pts. None of the local recurrences was localized in the surgical flap. An accurate mapping of recurrences location and absorbed dose to the surgical flap is currently ongoing.

Conclusions: In the analyzed cohort, none of the primary tumor recurrences occurred within the surgical flap. This finding could suggest that flaps does not represent an area at high risk of relapse. Further investigations are required to assess if it would be safe to avoid flap irradiation after a compartmental surgical approach.

Table 1. Patients data.

		Patients with local recurrence	Patients without local recurrence	Total number of patients
		n=28	n=155	n=183
Patients characteristics	**Gender**			
	Male	23	111	134
	Female	5	42	47
	Smoking habits			
	No	5	48	53
	Yes	23	107	130
	<= 20 pack year	5	42	47
	> 20 pack year	18	65	83
Surgical procedures	**Glossectomy**			
	IIIA-B	11	84	95 (52%)
	IVA-B	8	31	39 (21%)
	V	1	7	8 (4%)
	VI	8	33	41 (23%)
Tumor characteristics	**Grade**			
	G1 / G2 / G3	3/9/16	17/68/70	20/77/86
	Histological DOI (mm)			
	>10 / <=10	24/4	134/21	158/25
	Margin			
	Free/Positive/Close	23/2/3	124/14/17	147/16/20
	Margin Midline infiltration			
	Yes / No	3/2	6/25	9/27
	T-N Tract			
	Negative / Positive	22/6	127/28	149/34
	Vascular infiltration			
	Yes / No	2/26	11/144	13/170
	Perineural infiltration			
	Yes / No	4/24	35/120	39/144
	Intrinsic muscle infiltration			
	Yes / No	25/3	152/3	177/6
	Extrinsic muscle infiltration			
	Yes / No	23/5	136/19	159/24
	ECE			
	Yes / No	13/15	55/100	68/115
Staging (7th Ed TNM)	**Stage**			
	pT1-2	2	16	18
	pT3-4	26	139	165
	pN0-1	8	81	89
	pN2	20	72	92
	pN3	0	1	1
Staging (7th Ed AJCC)	III	1	4	5
	IVa	27	151	178

CO11

ADAPTIVE VOLUMETRIC MODULATED ARC RADIATION THERAPY FOR HEAD AND NECK CANCER: EVALUATION OF BENEFIT ON TARGET COVERAGE AND SPARING OF ORGANS AT RISK

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Aims: To investigate the dosimetric and clinical consequences of adaptive radiotherapy (ART) on patients with head and neck cancer (HNC) treated with Volumetric Modulated Arc Radiation Therapy.

Methods: We included in this retrospective analysis all the patients affected by HNC treated in our Institution with ART for radical or adjuvant intent. A pre-defined re-planning strategy was planned for cT3-4 or cN3 stage disease, or when a relevant weight loss or shrinkage of the primary tumor and/or nodal disease was observed at daily ConeBeam-CT. A new simulation CT scan was performed, together with a new thermoplastic mask, during the third week of RT course, followed by re-contouring of OARs and target volumes. The adaptive plan (APLAN) was produced with the modified set of structures and clinically delivered. For the study purpose, three different scenarios were considered as indicative to express the impact of the ART on the treated patients: first simulation CT and original plan (OPLAN), second simulation CT and adapted plan (APLAN) and second simulation CT and original plan (DPLAN). OPLAN was compared to APLAN and to DPLAN and the dosimetric differences for the targets and OARs were analyzed retrospectively.

Results: Fifty-six patients treated with ART from 2014 to 2021 were included. Patients' and disease's characteristics are summarized in Table 1. The non-adaptive DPLAN, when compared to OPLAN, showed increased dose to all OARs. Median spinal cord D2cc increased from 27.9 Gy to 31.4 Gy (p=0.00). The V15, V30 and V45 of DPLAN vs OPLAN increased by 21% (p=0.00), 15% (p=0.00), and 16% (p=0.00) for right parotid gland, and 16% (p=0.00), 19% (p=0.00), and 20% (p=0.00) for left parotid gland. A difference of 37% was observed for oral cavity V40 (p=0.00). Dose coverage was significantly reduced for both CTV (97.9% *vs* 99.9%; p=0.00) and PTV (94.7% vs 98.7%; p=0.00). The APLAN compared to OPLAN had similar results for all the considered OARs and showed the maintenance of both PTV (98.64% *vs* 98.72%; p=0.35) and CTV (99.91% *vs* 99.96%; p=0.30) coverage.

Conclusions: The adaptive strategy with re-planning during radiation therapy is able to avoid an increase of the dose to OARs and better target coverage in

HNC patients, with a potential benefit in terms of side effects and disease control.

Table 1. Patients' and disease's characteristics.

	N. (%)
Age at diagnosis, median (range)	69 years (39 – 95)
Sex	
Male	36 (64%)
Female	20 (36%)
Performance status	
0	15 (27%)
1	41 (73%)
Smoking	
Yes	22 (39%)
Ex-smoker	5 (9%)
No	29 (52%)
Primary tumor site	
Oral cavity	14 (25%)
Larynx	8 (14%)
Nasopharynx	2 (4%)
Oropharynx	17 (30%)
Hypopharynx	5 (9%)
Salivary glands	6 (11%)
Thyroid	2 (4%)
Paranasal Sinus	1 (2%)
Unknow primary	1 (2%)
Histology	
Squamous cell carcinoma	44 (79%)
Other	12 (21%)
Radiotherapy aim	
Radical	35 (62,5%)
Adjuvant	21 (37,5%)
Concomitant systemic therapy	
Yes	36 (%)
No	20 (35%)

CO12

ABSTRACT NOT PUBLISHABLE

CO13

EXTERNAL VALIDATION OF THE HEMO-EOSINOPHILS-INFLAMMATION INDEX AS A PROGNOSTICATOR IN ANAL CANCER: A MULTICENTRIC STUDY OF THE GASTROINTESTINAL WORKING GROUP OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Background and Purpose: A prognostic scoring system based on laboratory inflammation parameters, [Hemo-Eosinophils-Inflammation (HEI) index], including baseline hemoglobin level, the systemic inflammatory index and eosinophil count was recently proposed. HEI was shown to discriminate disease-free (DFS) and overall (OS) survival in ASCC treated with concurrent chemoradiation (CHT-RT). We tested the accuracy of the model on a multicentric cohort for external validation.

Materials and Method: Patients treated with CHT-RT were enrolled. The Kaplan–Meier curves for DFS and OS based on HEI risk groups were calculated and the log-rank test was used. Cox proportional hazards models were used to assess the prognostic factors for DFS and OS. The exponential of the regression coefficients provided an estimate of the hazard ratio (HR). For model discrimination, we determined Harrell's C-index, Gönen & Heller K Index and the explained variation on the log relative hazard scale.

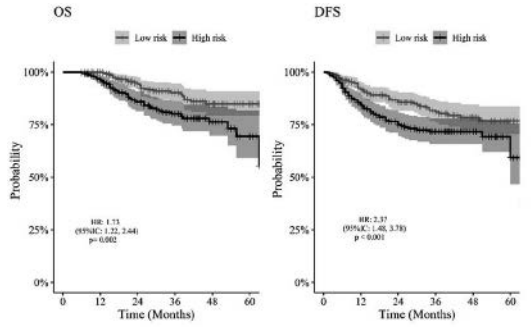

Figure 1.

Results: A total of 877 patients was available. Proportional hazards were adjusted for age, gender, tumor stage, chemotherapy. Two-year DFS was 77%(95%CI:72.0-82.4) and 88.3%(95%CI:84.8-92.0%) in the HEI high- and low- risk groups. Two-year OS was 87.8%(95%CI:83.7-92.0) and 94.2%(95%CI:91.5-97) (Figure 1). Multivariate Cox proportional hazards model showed a HR=2.02(95%CI:1.25-3.26;p=0.004) for the HEI high-risk group with respect to OS and a HR= 1.53(95%CI:1.04-2.24;p=0.029) for DFS. Harrel C-indexes were 0.68 and 0.66 in the validation dataset, for OS and DFS. Gonen-Heller K indexes were 0.67 and 0.71, respectively.

Conclusions: The HEI index proved to be a prognosticator in ASCC patients treated with CHT-RT. Model discrimination in the external validation cohort was acceptable.

CO14

DOWNSTAGING COULD BE CONSIDERED AN EARLY PREDICTOR OF SURVIVAL OUTCOMES IN RECTAL CANCER: RESULTS OF A POOLED DATASET OF RANDOMIZED TRIAL

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Aims: Several studies have shown that downstaging is a potential early predictor of neoadjuvant chemoradiation (nCRT) efficacy for locally advanced rectal cancer (LARC) patients. Downstaging could be defined as a reduction in T-category, N-category or pathological stage of disease compared to preoperative, but its impact on survival outcomes is still to be defined. The aim of this study is the evaluation of downstaging impact on survival outcomes in a pooled dataset of several randomized trials of nCRT in LARC.

Method: Patients from 8 large international rectal cancer trials (Accord 12/0405, EORTC 22921, FFCD 9203, CAO/ARO/AIO-94, CAO-ARO-AIO-04, INTERACT, I-CNR-RT, TROG 01.04) were included in a pooled analysis. Inclusion criteria were: age ≥18 years, nCRT treatment with or without adjuvant chemotherapy (CT) followed by surgery, and availability of information on at least one of clinical and pathological T-, N-, or downstaging. Metastatic patients or those who underwent conservative surgery approach were excluded from the analysis. Overall survival at 5 years (5yOS), distant metastasis free survival at 2 years (2yDMFS) and disease free survival at 2 years (2yDFS) rates were calculated using Kaplan Meier analysis. Patients were defined as downstaged when the difference of clinical and pathological stages (respectively on T value, N value and the TNM stage) was greater than or equal to 1. Kaplan Meier curve, Logrank test and univariate logistic regression were used for data analysis. A p-value less than 0.01 was considered as a statistically significant value.

Results: Overall, 4167 of 9564 LARC patients satisfied the inclusion criteria of this pooled dataset and were

finally analyzed. Out of all patients, the 5yOS was 78% (95% CI: 76.80 - 79.70), the 2yDMFS was 81.1% (95% CI: 79.80 - 82.30) and the 2yDFS was 80.8% (95% CI: 79.60 - 82.10). OS, DMFS and DFS are significantly higher in T-, N-, or stage- downstaged patients (p<0.01). 5yOS, 2yDMFS and 2y DFS were statistically significantly associated (p<0.01) with the downstaging of LARC patients assessed by T-status, N-status and disease stage.

Conclusions: According to the findings obtained in the pooled analysis presented in the current study, downstaging was favorably associated with all survival and disease control outcomes. Further analysis on this endpoint could lead to the identification of different disease subgroups that could benefit from targeted treatment strategies in the perspective of personalized medicine.

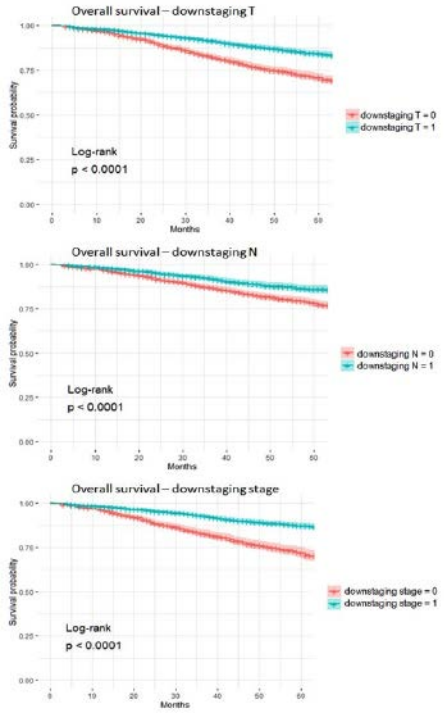

Figure 1.

CO15

TOTAL NEOADJUVANT THERAPY IN HIGH RISK RECTAL CANCER: A MULTICENTRIC RETROSPECTIVE STUDY ON BEHALF OF AIRO (ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY) GASTROINTESTINAL STUDY GROUP

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Aims: to report an Italian experience in the use of Total Neoadjuvant Therapy (TNT) in high risk locally advanced rectal cancer (LARC) patients (pts) and assess compliance, toxicity end efficacy.

Methods: pts with mid or low LARC staged as cT3N2 or cT4N0-2 or with mesorectal fascia infiltration (MRF+) receiving TNT were retrospectively included. TNT programs included induction(iCT) and/or consolidation (cCT) chemotherapy, long course chemoradiation(LC-CRT) or short course radiotherapy(SCRT). Pts compliance, toxicity, postoperative complication and response (Mandard Tumor Regression Grade-TRG) were reported.

Results: From 2005 to 2022, 166 pts underwent to TNT (median age 62 years) in 14 italian centers. 61(37%) pts had T3N2 disease, 47(28%) T3N1, 58(35%) T4; 110 pts(66.3%) had MRF+; 117 pts(70%) had a distal location. All but 15 pts received MRI and CT scan staging. 81(48.8%) pts underwent iCT and LC-CRT, 2 (1.2%) iCT and SCRT; 25(15%) LC-CRT and cCT, 9 pts(5.4%) received SCRT and cCT; 49(29.6%) pts received both iCT and cCT and LC-CRT. The most commonly used cCT and iCT regimen was CAPOX(48.8% and 57.3% respectively) and the median number of cycle was 3. Of the 155 pts receiving LC-CRT,68 (43.8%) had a dose intensificated LC-CRT with a median boost dose of 54 Gy; the most commonly used RT technique was VMAT. Among the 132 pts who received iCT, 8 (6%) required a dose modification, 6(4.5%) needed interruption and 3(2.3%) delayed cycles. Toxicity ≥G3 was reported in 5(3.8%) pts. 126(81.3%) pts completed LC-CRT without any interruptions, 13(8.3%) required concomitant CT dose reduction. Among 29 pts who required LC-CRT interrup-

tions, 25(86.2%) received iCT. Among the 82 pts who received cCT, 10(12%) required a dose modification, 1 needed interruption, 4(4.9%) delayed cycles. Toxicity≥G3 was reported in 2(2.4%) pts. Surgery was performed in 146 pts after a median of 14 weeks (IQR:11-19) from RT. R0 resection was performed in 116 pts(79.4%). Postoperative complications occurred in 33 pts. Pathologic response was available for 127 pts, TRG1 was reported in 23(18%). Considering the different programs, TRG1 rates achieved after iCT and LC-CRT; LC-CRT and cCT; iCT, LC-CRT and cCT were 13.5%, 20% and 14.2% respectively. 2-year OS and DFS were 89% and 64.3% respectively.

Conclusion: In high risk LARC pts Italian Centers proposed different TNT programs, iCT was the most common modality used. Compliance showed to be good. Efficacy requires further confirmation.

CO16

VALIDATION OF FOKAS ET AL. OUTCOME MEASURES IN RECTAL CANCER BY A POOLED ANALYSIS BASED ON INTERNATIONAL RANDOMIZED TRIALS OF 5473 PATIENTS

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Aims: Different endpoints are used in phase 2 and 3 rectal cancer studies. This large variability leads to inconsistency and difficulty in data interpretation. This important heterogeneity has led to the need for recommendations to define early and intermediate endpoints as a measure of overall survival (OS) in rectal cancer by Fokas et al. The purpose of this study is to validate, through a pooled analysis of international randomized trials in rectal cancer, the Fokas et al. recommendation.

Method: Pooled and treatment subgroup analysis were performed on 11 large international rectal cancer trials: Accord 12/0405, Dutch trial, EORTC 22921, FFCD 9203, CAO/ARO/AIO-94, CAO-ARO-AIO-04, CHRONICLE, INTERACT, I-CNR-RT, Polish II and TROG 01.04. All the selected patients were > 18 years old and received short course (SC-RT) or long-course radiotherapy (RT) (LG-RT) with or without concomitant and/or adjuvant chemotherapy (CT) followed by surgery. Metastatic patients or those who underwent conservative surgery, such as minimally invasive transanal excision (TAMIS) or transanal endoscopic microsurgery (TEM), were excluded from the analysis. Several variables (both early, such as clinical staging, tumor location, surgical interval ≥ 12 weeks, the downstaging of TNM, of the tumor and of the lymphnodes, neoadjuvant rectal (NAR) score, surgical procedure and intermediate, such as local recurrence and distant metastases) were correlated with the 5- years OS. Pearson's Chi-squared test was used for data analysis and a p-value less than 0.01 was considered as a statistically significant value.

Results: A total of 5473 patients (1718 female and 3752 male) out of 9564 met the inclusion criteria and were finally analyzed. All patients completed the RT course, of whom 988 (18%) underwent SC-RT and 4485 (82%) underwent LC-RT. For the entire sample, 2-year disease-free survival (DFS) was 80% (79-82%), 3-year DFS was 77% (75-78%), and 5-year overall survival (OS) was 75% (74% to 77%). Results regarding early and intermediate endpoints on 5-years OS, with their respective statistical significance, are described in Table 1.

Conclusions: This pooled analysis of 5473 patients with rectal cancer confirms the correlation reported by Fokas et al. between intermediate endpoints and OS. This suggests that these early and intermediate endpoints could be used as primary or secondary outcomes for the design of prospective clinical trials in rectal cancer.

Table 1.

Endpoints	5 years -OS	
	R	p
cTNM	0,13	<0,01
Tumor location	-0,07	0,01
Surgical interval ≥ 12weeks	-0,03	1,00
Downstaging TNM	-0,21	<0,01
Downstaging T	-0,21	<0,01
Downstaging N	-0,04	1,00
pCR	-0,10	<0,01
Lymphnode status	-0,24	<0,01
NAR score	0,30	<0,01
Surgical Procedure	-0,11	<0,01
Local recurrence	0,41	<0,01
Distant metastasis	0,57	<0,01

CO17

THE PROGNOSTIC VALUE OF THE SIZE AND THE SITE OF THE LOCAL FAILURE AT DCE-MRI BEFORE SALVAGE RADIOTHERAPY FOR PROSTATE CANCER

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Aims: To investigate predictors of biochemical failure after salvage radiotherapy (sRT) in the context of a presumed local failure at dynamic contrast-enhancement-magnetic resonance imaging (DCE-MRI) post radical prostatectomy (RP).

Methods: From January 2014 patients with biochemical failure were restaged with both PET/CT and multiparametric MRI; those with a presumed local failure at 3T DCE-MRI as well as no regional/distant disease at PET/CT (either choline and/or PSMA) were included. History of androgen deprivation (AD) before sRT and positive nodes at RP were considered exclusion criteria. The lesion(s) identified on DCE-MRI were transferred on planning CT after co-registration. sRT consisted in 73.5 Gy to the presumed local lesion and 66-69 Gy to the prostatic bed in 30 fxs. Pelvic nodes (PN) were covered to 54 Gy/30 fxs in selected patients. The endpoint of the study was the development of a biochemical failure after sRT defined as a 0.2 ng/ml PSA rise above the nadir. Various covariates regarding patient and disease characteristics were investigated at univariate analysis (UVA) on the time to biochemical failure (bNED-survival). Covariates with a p value <0.2 at UVA were entered a Cox proportional hazards regression analysis.

Results: Up to June 2020, 146 patients have been included in the study. Median (IQR) PSA at sRT was 0.60 ng/ml (0.38-1.05 ng/ml) and only 17 patients (11.6%) received AD along with sRT. A total of 168 local lesions have been detected, 92 (54.8%), 40 (23.8%) and 36 (21.4%) at the vesicourethral anastomosis (VUA), the bladder neck and the retrovesical space, respectively. At the median (IQR) follow-up of 48.1 mths (31.3-60.6 mths), 22 biochemical failures occurred for a 4-yr bNED survival of 84.4% (95%CI: 77.9-90.9%). On UVA, bNED-survival after sRT was significantly more likely for patients with VUA-only lesions (VUA-only vs others, HR=0.307, 95%CI: 0.120- 0.784, p=0.014) and with smaller lesions (for every cc, HR: 1.071, 95%CI: 1.025-1.119, p=0.002). For patients with VUA-only disease or with lesions smaller than 0.5cc, 4-yr bNED survival rates were 90.7% (95%CI: 83.4-98.0%) and 90.6% (95%CI: 83.9-97.3%), respectively. The 46 patients with both favorable features had a 4-yr bNED rate of 94.6% (95%CI: 87.3-100%).

Conclusions: These data support local restaging with DCE-MRI before sRT for biochemical failure after RP. Patients with VUA-only and/or small volume lesions have an excellent outcome after dose-escalated sRT.

CO18

POST-PROSTATECTOMY ABLATIVE RADIATION THERAPY (POPART): A MULTICENTRIC PROSPECTIVE ITALIAN TRIAL

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Aims: To investigate the feasibility of ultrahypofractionated radiotherapy to prostate bed in patients with biochemical and/or clinical relapse following radical prostatectomy enrolled in the prospective observational multicentric POPART trial (NCT04831970).

Method: Patients with post-radical prostatectomy PSA level of ≥ 0.1-2.0 ng/mL or local relapse at PSMA PET CT or multiparametric MRI were treated with Linac-based Volumetric Modulated Arc Therapy (VMAT) on prostate bed up to a total dose of 32.5 Gy in five fractions every other day (EQD21.5 = 74.2 Gy). Androgen deprivation therapy (ADT) was allowed at physician's discretion. Maximum acute toxicity was assessed with Common Terminology Criteria for Adverse Events version 5 (CTCAE_v5) scale. In addition International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) score was used at baseline and during the follow-up.

Results: From April 2021 to May 2022 thirty-three men with a median age of 72 years (range 59-82) were enrolled in three Italian centres. The majority of them (76%) had a biochemical relapse only, while 8 patients (24%) had a local relapse. Median PSA level before RT was 0.24 ng/ml (range 0.18-1.89 ng/ml). Four patients (12%) received ADT. At baseline median ICIQ-SF score was 1 (range 0-8). The median PTV was 60.1 cc (range 25.9-240 cc). No treatment interruptions were registered. Only one instance of Grade 2 acute gastrointestinal (GI) toxicity was documented. No ≥ Grade 2 acute genitourinary (GU) toxicity was observed, and 3 patients experienced Grade 1 GU side effects. No significant changes in ICIQ-SF were assessed. At the time of analysis, all patients were biochemically controlled with a median post-treatment PSA level of 0.06 ng/ml (range 0-0.95 ng/ml), except one who showed a pelvic (nodal) recurrence.

Conclusions: Post-prostatectomy ablative radiation therapy to the prostate bed for biochemical and/or clinical

relapse allowed a convenient and safe treatment with negligible early side effects. This regimen can be an attractive strategy to reduce the burden of care without losing clinical effectiveness, provided that long term results will confirm these findings.

CO19

PRELIMINARY RESULTS OF PRO-EPI: PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY ON ELECTIVE PELVIC NODAL IRRADIATION FOR NON-METASTATIC PROSTATE CANCER UNDERGOING RADICAL, ADJUVANT OR SALVAGE RADIOTHERAPY WITH OR WITHOUT ANDROGEN DEPRIVATION THERAPY

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Aims: Although radiotherapy plays a crucial role in the management of intermediate/high/very high risk non-metastatic prostatic cancer (IHR-nmPca), there is still no consensus on the optimal treatment strategy in this setting. Remarkably, the indication to elective pelvic radiotherapy (ENI) is still highly controversial. The PROspective multicenter observational study on Elective Pelvic nodes Irradiation (PRO-EPI) was designed to provide "real life" data regarding the patterns of care for IHR-nmPca.

Methods: Forty-three Italian Radiation Oncology centers participated in the PRO-EPI project, with 1029 patients enrolled. In this preliminary analysis we longitudinally evaluated the impact of ENI and radiotherapy features on toxicity and quality of life (QoL). Six months follow-up data were available for 913 patients and 12 months data for 762 patients.

Results: Elective Nodal Irradiation was given to 506 patients (48.9%). Volumetric Intensity-Modulated Radiation Therapy (IMRT) was adopted in more than 77% of patients and Image-Guided Radiation Therapy (IGRT) in 84.4%. Androgen deprivation therapy (ADT) was administered to the majority of patients (68.3%) and it was associated to ENI in 408 cases. Toxicity was mostly mild and reversible and IGRT resulted in a significant reduction of rectal toxicity, although a non-significant trend towards increased urinary toxicity was observed. No statistically significant differences in QoL and toxicity were seen between patients treated with or without ENI.

Conclusions: The adoption of IGRT is widespread and constantly increasing and could reduce treatment toxicity. ENI is not yet the standard treatment, but it is performed in a growing fraction of cases and did not result in greater toxicity or worse QoL. Further analyses are needed to clarify the long-term toxicity profile and the impact of ENI on progression free survival and overall survival.

CO20

IMAGE-GUIDED STEREOTACTIC BODY RE-IRRADIATION OF PROSTATE CANCER RECURRENCE: PRELIMINARY REPORT OF A MONOISTITUTIONAL STUDY

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Aims: Management of locally recurrent prostate cancer after definitive radiotherapy remains controversial . The aim of this study is to explore the efficacy and safety of prostate re-irradiation with image-guided stereotactic volumetric modulate arc radiation therapy (VMAT-IGRT). We present our preliminary results.

Methods: Men affected by isolated local recurrence of prostate cancer, proven by a 18F-Choline or PSMA positron emission tomography and 3Tmultiparametric magnetic resonance, who underwent previous prostate external beam radiation therapy were enrolled in this study. Between may 2018 and June 2022 19 pts were re-irradiated to the prostate with stereotactic VMAT-IGRT, the total dose was 30Gy in 5 daily fractions. Pts were followed by clinical examination and PSA value 1 month after treatment and every 3 months thereafter. The primary outcome is to estimate the efficacy of the salvage stereotactic VMAT-IGRT in terms of biochemical relapse-free survival (bRFS), local control (Lc), and androgen deprivation therapy free interval (ADTFI). Secondary outcomes are acute and late genitourinary and gastrointestinal toxicities evaluated according to Common Terminology Criteria for Adverse Events version 4.03.

Results: After a median follow-up of 23 months (range 15-48), 18 of 19 pts accrued were evaluable. No G3 acute urinary toxicity was registered, gastrointestinal acute toxicity was negligible. In the first six months all but two pts had a decrease in serum level PSA, three pts had a progressive increase in serum PSA at the ninth, twelfth and fifteenth months, respectively. The five pts with biochemical failure showed bone or nodal progression without evidence of local recurrence at choline or

PSMA PET.

Conclusions: Our preliminary report showed that stereotactic V-MAT-IGRT re-irradiation could be a safe and effective treatment in selected pts with local recurrence prostate cancer, with an excellent acute toxicity profile.

CO21

SHORT-TERM RT FOR EARLY PCA WITH CONCOMITANT BOOST TO THE DIL (PHASE II TRIAL AIRC-IG-13218) - A 5 YEAR UPDATE

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Aims: The purpose of the study is to report updated toxicity and oncological results at 5 years of the Phase II prospective trial "Short-term high precision radiotherapy for early prostate cancer with simultaneous boost to the dominant intraprostatic lesion (DIL) for patients with early stage prostate cancer (PCa)".

Methods: The study enrolled 65 patients since June 2015. Patients with low and intermediate risk PCa meeting the inclusion criteria underwent extreme hypofractionated radiotherapy to the prostate (36.25 Gy in 5 fractions) and a simultaneous integrated boost to the DIL of 37.5 Gy; which was identified by a multiparamentric MRI (mpMRI) co-registered with the planning CT. Toxicity was assessed according to CTCAE v4.0, RTOG and EORTC criteria. Quality of life (QoL) of contacted and alive patients was assessed by International Prostate Symptoms score (IPSS), European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire—Core 30 (EORTC QLQ-C30), EORTC QLQ prostate specific (QLQ-PR25), and sexual activity by International Index of Erectile Function (IIEF-5). For all patients with no evidence of disease (NED), prostate-specific antigen (PSA) values were collected and analysed.

Results: Five-years follow-up was available for 50 out of the 65 enrolled patients. After a median follow-up of 4.8 years (IQR 3.8-5.2 years), out of the 50 reachable patients, 40 (73%) resulted alive with NED, 3 (8%) alive with disease and 7 (19%) died for other causes. Biochemical progression-free survival at 5 years calculated on all patients and on patients still alive was 73% and 90%, respectively. Overall survival at 5 years was 81%. Out of the 40 NED patients, median PSA was 0.36 ng/ml (IQR 0.18-0.63 ng/ml). One grade (G) 1 and two G2 gastrointestinal (GI) and 8 G1 and 2 G2 genitourinary (GU) toxicities were reported, no G≥3 events were reported. Questionnaires showed that patients' overall QoL was satisfactory at last follow-up.

Conclusions: These updated data about efficacy and late toxicity confirm our previously published findings that extreme hypofractionated schedule with concomitant boost on the DIL is a safe and effective approach. The increasing dose to the DIL does not worsen the RT toxicity and consequently does not affect patients' QoL, thus opening for the possibility of an even more escalated treatment.

CO22

DOSIMETRIC IMPACT OF INTRAFRACTION PROSTATE MOTION IN DOSE-ESCALATED LINAC-BASED SBRT

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Aims: The aim of this study was to investigate the impact of intrafraction prostate motion on dose metrics and the effect of beam gating and motion correction in dose-escalated linac-based SBRT.

Method: Thirteen patients (56 fractions) underwent dose-escalated SBRT using FFF–VMAT technique. Real-time 3D prostate motion data were acquired using a novel electromagnetic tracking device. Treatment was interrupted when the signals exceeded a 2 mm threshold in any of the three spatial directions and couch position corrected unless the offset was transient. Prostate trajectories with and without beam gating and motion correction events were reconstructed and analyzed. Both actually delivered treatments (case A) and non-gated treatments (case B) were simulated by incorporating the observed prostate motion for each fraction into the patient original plan with an isocenter shift method. Target and organs at risk (OARs) dosimetric parameters of the two motion-inclusive plans were compared to planned values and protocol dose constraints. A Wilcoxon-Mann-Whitney test (alpha=0.05) was performed to assess statistical significance.

Results: Treatment interruptions were needed in 25 fractions (45%) due to target motion beyond the predefined threshold. Average values of mean prostate displacements in case A were -0.2 mm [-1.6–0.8], 0.1 mm [-1.4–1.5], and -0.3 mm [-1.7–1.4] in lateral, longitudinal, and vertical directions, respectively. The same values in case B were -0.3 mm [-3.1–0.8], 0.0 mm [-4.2–3.7], and -0.6 mm [-3.5–1.9]. Mean relative dose differences were 0.0% [-1.8–1.1] for CTV D99% and -0.2% [-1.6–0.8] for PTV D95% in case A, and -1.2% [-8.8–0.8] and -1.1% [-6.3–0.7] in case B. In both cases, urethra planning organ at risk volume was slightly degraded after taking motion

into account, and rectum and bladder dose metrics showed a favorable underexposition of the rectum and an undesirable overdose to the bladder. Nevertheless, no protocol dose constraints violations were observed. The dosimetric comparison relative to the planned dose wasn't statistically significant (p>0.05) both for case A and case B.

Conclusions: The current CTV-to-PTV margins, the robustness of original treatment plans, and the fast FFF beams delivery led to minimal degradations of dose metrics for the target and OARs in both cases. Anyway, real-time monitoring with beam gating and motion correction ensured superior results and are recommended in dose-escalated prostate SBRT.

CO23

MRI SENSITIVITY IN DETECTING MACROSCOPIC LOCAL RECURRENCES IN PROSTATE CANCER PATIENTS WITH PLANNED SALVAGE RADIOTHERAPY: AN OBSERVATIONAL STUDY

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Aims: Biochemical recurrence of prostate cancer after radical prostatectomy are recorded in approximately 15 to 30% of cases. Treatment options are represented by salvage radiotherapy (SRT), hormonal therapy, or observation with PSA level monitoring. In patients eligible for SRT, current guidelines recommend PSMA PET to exclude distant metastases. An observational study of our centre (ICAROS) was carried out to evaluate a possible role of MRI before SRT. Aim of this report was to describe the preliminary results.

Method: Over a 4-year period, all patients eligible to SRT without contraindications to MRI underwent clinical and instrumental examination including pelvic multiparametric MRI with endorectal coil, possibly associated with choline or PSMA PET. The following data were prospectively collected: PSA at biochemical relapse, PSA doubling time, ISUP score, SRT treatment plan, site and size of any macroscopic recurrence, outcome.

Results: Fifty-eight patients were evaluated in this study. Median age was 64 years (range: 41-78), median PSA level at biochemical recurrence was 0.66 ng/ml (range: 0.12-6.24), and most patients (68.9%) had ISUP 3-5. Pre-SRT MRI was positive for local recurrence in 40/58 patients (68.9%), for pelvic nodal metastases in 1/58 (1.7%), and for pelvic bone metastases in 1/58 (1.7%). The site of local recurrence was as follows: bladder neck 30/42 (71.4%), vesicourethral anastomosis 7/42 (16.7%), rectovesical space 2/42 (4.8%), prostatic fossa 1/42 (2.4%). Twenty-eight patients (66.7%) with positive MRI also underwent choline or PSMA PET. Of these, only 9 patients (21.4%) showed the same uptake at the same sites as evidenced by MRI. Conversely, in 19 patients (45.2%) MRI results did not match the PET result.

Conclusions: An unexpectedly high rate of macroscopic local relapse was recorded in a cohort of patients with biochemical recurrence after radical prostatectomy and prospectively assessed with MRI. These results challenge current recommendations on the most appropriate imaging exams in this clinical setting.

CO24

A PROSPECTIVE STUDY ASSESSING THE PATTERN OF RESPONSE OF LOCAL DISEASE AT DCE-MRI AFTER SALVAGE RADIOTHERAPY FOR PROSTATE CANCER

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Aim: To assess the pattern of response of presumed local lesions at dynamic contrast enhancement magnetic resonance imaging (DCE-MRI) in the setting of salvage radiotherapy (sRT) after radical prostatectomy (RP).

Methods: The present prospective study was conducted at a single Institution between August 2017 and June 2020. Eligibility criteria were: undetectable prostate specific antigen (PSA) after RP; biochemical recurrence (2 consecutive PSA rises to 0.2 ng/ml or greater); a presumed local failure at DCE-MRI (early/fast enhancing discrete lesion on DCE sequences); no distant metastases at choline-PET/CT; no previous history of androgen deprivation therapy and/or RT. Accrued patients underwent exclusive sRT delivering 66–69 Gy and 73.5 Gy in 30 fractions to the whole prostatic fossa and to the local failure(s) detected at DCE-MRI, respectively and when treated, 54 Gy/30 fractions to the pelvic nodes. All patients were offered DCE-MRI at 3 months intervals after sRT until complete disappearance (CR) of the lesion(s) or up to a maximum of 4 revaluations. The endpoint of the study, complete response (CR), was defined as the complete disappearance of the target lesion at DCE-MRI.

Results: 62 patients with 72 nodules were enrolled. All patients underwent the 1st revaluation at a median of 3.3 months (IQR: 3.1-4.1), and 33 patients (53.2%) showed a CR. The median time to CR was 4.7 months. Four patients did not undergo further testing before achieving a CR and even considering these patients as no responses, the vast majority (87.1%, 95%CI: 78.5–94.4%) of lesions would have completely disappeared by 12 months from the end of sRT. The volume of the lesion

at pre-sRT DCE-MRI was an independent predictor of CR at the 1st revaluation (OR: 0.076, 95%CI: 0.009–0.667; p = 0.020) along with time elapsed from sRT (OR: 3.399, 95% CI: 1.156–9.993, p = 0.026).

Conclusion: The present study documents the complete disappearance of the vast majority of local lesions after dose-escalated sRT though this requires several months after sRT; timing of CR is at least in part predictable based on the volume of the lesion.

CO25

STEREOTACTIC ABLATIVE RADIOTHERAPY IN NEWLY DIAGNOSED AND RECURRENT LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS UNFIT FOR CONCURRENT RADIO-CHEMOTHERAPY: EARLY ANALYSIS OF THE START-NEW-ERA NON-RANDOMISED PHASE II TRIAL

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Purpose: This is a single arm phase 2 study (Clinical trials.gov NCT05291780) to assess local control (LC) and safety of stereotactic ablative radiotherapy (SABR) in unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients unfit for concurrent chemoradiotherapy (ChT-RT).

Methods and materials: Neoadjuvant ChT was prescribed in fit patients. The tumor volume included primary tumor (T) and any regionally positive node/s (N). The co-primary study endpoints were LC and safety.

Results: Between December 31, 2015 and December 31, 2020 50 LA-NSCLC patients were enrolled. Histology was squamous cell carcinoma (SCC) and adenocarcinoma (ADK) in 52% and 48%, respectively. 40 (80%) patients had ultra-central tumor. Twenty-seven (54%) received neoadjuvant ChT and 7 (14%) adjuvant Durvalumab. Median prescribed dose was 45 Gy (range, 35-55) and 40 Gy (35-45) in 5 daily fractions to T and N, respectively. After a median follow-up of 38 months (range, 12-80), 19 (38%) patients had experienced local recurrence (LR) at a median time of 13 months (range, 7-34). The median LR-free survival (FS) was not reached (95% CI, 28 to not reached). The 1-, 2- and 3- year LR-FS rates were 86±5%, 66±7% and 56±8%, respectively. At last follow-up, 33 (66%) patients were alive. Median overall survival (OS) was 55 months (95% CI, 43-55 months). The 1, 2, and 3-year OS rates were 94±3%, 79±6% and 72±7%, respectively. No patients developed ≥ grade (G) 3 toxicity. At multivariate analysis ADK (p 0.03) resulted significant predictor of better LC, while OS was significantly conditioned by smaller PTVs (p 0.008) and TNM stage (p 0.016).

Conclusions: LA-NSCLC patients treated with SABR had optimal LC and promising OS in absence of ≥G3 toxicity. Our early outcomes would suggest the feasibility of using this approach in LA-NSCLC patients unfit for concurrent ChT-RT.

CO26

NON-METASTATIC MALIGNANT PLEURAL MESOTHELIOMA PATIENTS TREATED WITH LUNG-SPARING SURGERY, CHEMOTHERAPY AND RADICAL HEMITHORACIC RADIOTHERAPY: LONG TERM RESULTS FROM A PHASE III RANDOMIZED CLINICAL TRIAL

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Aims: Aim of this paper is report the long-term survival and toxicity outcomes for malignant pleural mesothelioma (MPM) patients treated with lung-sparing surgery (LSS), chemotherapy (CT) and Radical Hemithoracic Radiotherapy (RHR). Previously published phase III randomized clinical trial demonstrated significant advantages of RHR compared to palliative radiotherapy (PR) in terms of overall survival.

Methods Patients with histologically proved MPM, who underwent non-radical LSS and CT were treated with RHR. Kaplan Meier analyses were performed to assess the median overall survival (OS), local and locoregional recurrences (LRRR), distance recurrence (DRR), defined as the time intercourse since the end of RHR to death from any causes, LRRR, DRR or the end of the study (May 2022). Acute and late toxicity rates were reported. Patients were subdivided in groups according to pathological staging, primary tumor (T) and nodal status (N) to identify prognostic factors. The log-rank test (two-sided) was used to test OS differences between patients with T1-T2 *vs* T3-T4; N2 vs N0-N1 and pathological staging I-II vs III-IV. The Gray's test was used to evaluate hypothesis of equality of cumulative incidence of local recurrence and distant metastases for the same groups of patients.

Results: From August 2014 to May 2018, 55 patients were treated with RHR. After a median Follow-up period of 35 months, the median OS was 22,8 months, the 1, 2 and 3-years OS rates were 76%, 45% and 30%, respecti-

vely. The 3-years rate of LRRR and distant metastases were 33% and 55%. The median OS for patients with pN2 disease was 14,5 months vs. 23 months for the group N0-N1 (p 0,229), with no difference in the 3-years LRRR rates (38% *vs* 32%). Patients with T1-T2 disease had the better prognosis with a median survival of 27.8 months. Toxicity rate was significant. Overall, 17 patients (31%) experienced Grade 3 toxicity. Most of them (11/17 cases, 65%) were related to lung damage: pneumonitis (7), fibrosis (3) and Thromboembolic event (1). Seven patients (13%) experienced Grade 3 toxicity during RT course and 1 patient (2%) died. Seven patients (13%) reported Grade 3 late- toxicity events: 5 pneumonitis, 1 fibrosis and 1 fatigue.

Conclusions: MPM is a rare disease with poor prognosis. According to this study, patients underwent trimodality treatment with LSS, CT and RHR had significant better prognosis compared to patients who received PR. Rate of toxicity was significant but acceptable

CO27

EVALUATION OF EARLY CARDIAC TOXICITY IN RADIOTHERAPY FOR STAGE III NON-SMALL CELL LUNG CANCER: PRELIMINARY ANALYSIS HEART DOSIMETRIC STUDY

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Aims: The aim of this study was to prospectively investigate a correlation between the heart dosimetry and early heart demage in patients with LA-NSCLC undergoing chemoradiotherapy (CRT).

Methods: This trial is a prospective, observational cohort study including patients with stage IIIA-IIIB NSCLC who underwent concomitant chemoradiotherapy (CRT). Radiotherapy was delivered with a median total dose of 60 Gy with conventional fractionation. The 3D techinique or Intesity-modulated radiotherapy (IMRT) was used. Manual contouring of target and organs at risk (OAR), was performed from the simulation CT images. The difference in cardiac dosimetry in patients who have experienced cardiac and no-cardiac events (CV) was assessed by T-Test. Subsequently, dosimetric parameters that resulted different between patients who experienced CV and patients who did not, were subjected to regression analysis.

Results: This preliminary analysis included thirty-four patients with stage IIIA-IIIB NSCLC. The median age was 69.5 years (range, 43-87). The median follow-up was 27.8 months. 62% of patients were in stage IIIA. All patients were treated with concurrent CRT and in 65% used a platinum-based regimen. No patients died of CV complications. Eight patients (23.5%) had a CV event: four atrial fibrillation, two supraventricular tachycardia, one atrioventricular block (second degree), and one patient presented heart failure. The cardiac dosimetric parameters analyzed were described in Table 1. The analysis of cardiac dosimetry shown in Table 2, patients who developed CV and no-CV have higher mean values of PTV volume (442 *vs* 310 p=0.031), heartDmean (17.72 *vs* 11.89 p=0.032), V30 (24 vs 13 p=0.009), V45 (10.79 *vs* 5.68 p=0.007), V50 (7 *vs* 3.85 p=0.030) resulting all predictive of CV events: PTV volume (AUC 0.75), HeartDmean (AUC 0.73), V30 (AUC=0.76), V45 (AUC=0.79) and V50 (AUC=0.72).

Conclusions: This preliminary data shown that all parameters evaluated, except left anterior descending artery (LAD) dose, were found to be predictive of cardiovascular damage after CRT in these patients. These results encourage us to continue the study in order to estimate the overall and individual incidence of any early cardiac event and to identify additional variables that cause an increased risk of acute cardiac events.

Table 1. Descriptive Statistics.

	N	Minimum	Maximum	Mean	SD
PTV Volume	34	124.94	748.33	341.17	153.78
Heart Dmax	34	51.96	108	61.86	9.25
Heart Dmean	34	3.38	31.04	13.26	6.79
V5	34	13.13	99.99	52.06	25.22
V30	34	1.38	48.27	16.05	11.04
V45	34	0.39	16.98	6.88	4.83
V50	34	0.10	12.36	4.59	3.65
LADDmax	34	2.67	49.61	23.63	15.33
LADDmean	34	1.02	31.03	8.97	7.27

Table 2. Differences in mean values between groups with CV and non-CV events.

	CV events (0 NO/1 SI)	Mean	SD	p-value	AUC
PTV Volume	0	310.02	140.40	P=0.031	0.755
	1	442.40	460.50		
Heart Dmean	0	11.89	5.86	P=0.032	0.736
	1	17.72	8.06		
V30	0	13.40	8.86	P=0.009	0.764
	1	24.67	13.53		
V45	0	5.68	4.09	P=0.007	0.793
	1	10.79	5.24		
V50	0	3.85	3.25	P=0.030	0.721
	1	7.00	4.02		

CO28

LOCALLY ADVANCED NSCLC: OVERVIEW OF PATTERN OF RECURRENCE IN DURVALUMAB ERA (LEOPARD TRIAL)

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Aim: The treatment outcome of locally advanced non-small cell lung cancer (LA-NSCLC) has been improved over the past years, however local failure is still common and represent the mail challenge.

Methods: LA-NSCLC patients (pts) treated with chemoradiotherapy (CCRT) and Durvalumab between January 2018 and December 2021 in 5 Italians Institutions were included. Primary endpoint is the pattern of recurrence in terms of:
- Oligoprogression (OPD) versus pluri-progression (PPD)
- In field-recurrence versus out-field recurrence

Secondary endpoints are: progression free survival (PFS) and overall survival (OS).

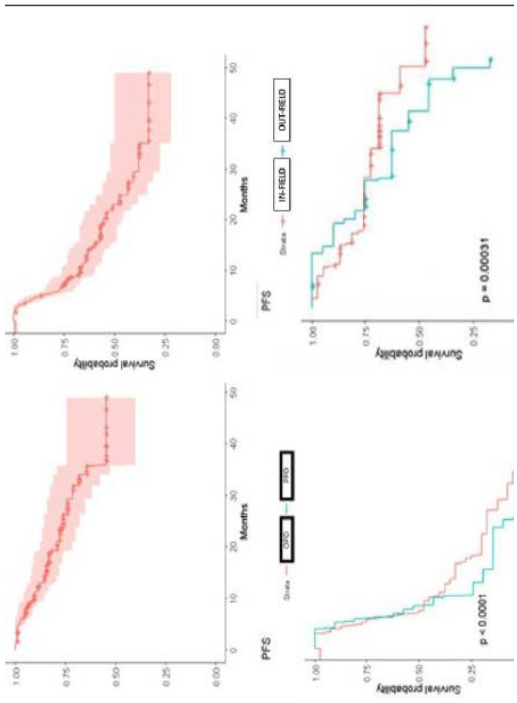

Figure 1.

Results: 132 pts met the inclusion criteria. The median age was 67 years. Majority of pts were males (92 pts). 88 (66.7%) and 44 (33.3%) were stage IIIA and stage IIIB NSCLC respectively. 92 (70%) pts were treated with CCRT; all pts receiving platinum-based doublet CT. The RT dose received by 121 (92%) pts was 60 Gy in 30 fractions; two pts received a total dose greater than 60 Gy and 9 pts a dose less than 60 Gy. All analyzed pts underwent at least one Durva maintenance course (mean cycles 14, range 1-27). The median follow-up was 17 months. At last follow up 60 (45%) pts experienced disease relapse, of which 32 pts during Durva treatment. Of these, 39 (65%) pts experienced OPD. Twenty pts experienced an in field relapse; of these 12 fell into the OPD and the remaining 8 in the PPD category. The salvage therapy in OPD group was RT alone or in combination with systemic therapy in 24 pts; most of these pts underwent stereotactic RT with a mean dose of 31 Gy (range, 21-60 Gy) in 1-5 fractions. At last follow up, 27 pts died, of which 20 for cancer related cause and 7 for other causes; two pts were lost to follow up and 103 are still alive. Median OS was not reached. The 1-, 2- and 3-year OS rate were 89 %, 76%, and 55%, respectively. The median PFS was 23 months. The 1-, 2- and 3-year PFS rate were 64%, 48%, and 33%, respectively. There was no difference in OS between ODP vs. poliPD and between in field vs. outfield recurrence; a difference in PFS between OPD and poliPD with a 1-year PFS of 33% and 19%, respectively was shown. A difference in PFS between pts who have a relapse in the field compared to those who have an out-field relapse is also evident with a 1-year PFS of 40% and 20%, respectively.

Conclusions: In Durva era, the OPD and in-field relapses are not uncommon after CCRT in LA-NSCLC and their management remains a clinical challenge.

CO29

THE PROGNOSTIC VALUE OF NEUTROPHILS TO LYMPHOCYTES RATIO (NLR) IN PATIENTS WITH STAGE III NSCLC TREATED WITH RADIO-CHEMOTHERAPY: A RETROSPECTIVE MULTICENTRIC ANALYSIS

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Aims: Neutrophils to Lymphocytes Ratio (NLR) is one of the most important host-related prognostic factors for many solid tumors. NLR demonstrated to be an independent prognostic factor of poor survival for advanced non-small cell lung cancer (NSCLC), in particular for EGFR mutated patients. Aim of this study is to evaluate

the prognostic value of NLR in stage III NSCLC treated with sequential or concomitant radio-chemotherapy.

Methods: Data from patients affected by stage III NSCLC treated with definitive radio-chemotherapy in 5 radiotherapy italian centers were retrospectively collected. NLR was obtained from the blood tests taken at the beginning and at the end of the radio-chemotherapy treatment. An univariate and a multivariate analysis using cox-regression test were performed in order to correlate NLR to patient clinical outcomes.

Results: One hundred and ten patients treated from 2016 to 2018 were enrolled, subsequently 25 of them were excluded for the lack of data on blood count. Patient characteristics are reported in Table 1. Different cut-offs of NLR (2-2.5-3-4-5) were correlated with Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS). At uni variate analysis only the NLR=2.5 was significantly related to OS: patients with NLR<2.5 presented an OS of 95.8% and 70.9% at 1 and 3 years respectively, vs an OS of 86.8% and 48.3% observed in patients with NLR>2.5 (p:0.05). On subgroups analysis higher NLR was related to stage IIIC NSCLC compared to stage IIIA and IIIB (p:0.488).

Conclusions: Our results showed that NLR>2.5 is a prognostic factor for poor OS for stage III NSCLC. Higher NLR was related to a higher disease burden (Stage III C). These findings confirm the prognostic value of NLR also for stage III NSCLC. Further analysis on patients receiving immunotherapy after radio-chemotherapy treatment will be analyzed from the "Neutrality trial" which is still ongoing.

Table 1. Patient and disease characteristics.

	Number of patients	% of patients
Age at diagnosis		
< 60	28	32.9
61-65	11	12.9
66-70	17	20
71-75	14	16.5
>76	15	17.7
PS ECOG		
0	51	60
1	34	40
Stage		
IIIA	37	43.5
IIIB	39	45.9
IIIC	9	10.6
Histology		
Adenocarcinoma	43	50.6
Squamous cell carcinoma	37	43.5
Mixted/Not differenciated	5	5.9
PDL 1		
Negative	8	9.4
<50	9	10.6
>50	3	3.5
Unknown	65	76.5

CO30

COMPUTED TOMOGRAPHY-BASED RADIOMICS IN OROPHARYNGEAL CANCER PATIENTS TREATED WITH RADIOTHERAPY: A PROMISING TOOL FOR OUTCOME MODELING

S. Volpe[1,2], F. Colombo[1,2], A. Gaeta[1], M. Pepa[1], M. Zaffaroni[1], M.G. Vincini[1], I. Turturici[1], A. Casbarra[1,2], G. Marvaso[1,2], A.M. Ferrari[1], R. Santamaria[1], M. Cremonesi[1], S. Raimondi[1], M. Ansarin[1], R. Orecchia[1], D. Alterio[1], B.A. Jereczek-Fossa[1,2]

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Aims: To assess whether CT-based radiomics could improve the prediction of overall survival (OS) and local progression free survival (LPFS) in patients (pts) with oropharyngeal cancer (OPC) treated with curative-intent IMRT.

Methods: Consecutive OPC pts with radiologically detectable primary tumor treated between 2005 and 2021 were included. Analyzed clinical variables included gender, age, smoking history, staging, subsite, HPV status and blood counts (*e.g.* baseline hemoglobin, platelets, and lymphocyte/monocyte ratio). Gross tumor volumes (GTVs) of the primary tumor were manually segmented; Pyradiomics was used for features extraction. For the analysis, univariate proportional hazard and penalized Cox regression models were applied to clinical and radiomic features, respectively; a radiomic score (RS) was obtained for prognostic stratification. Lasso regression was applied to select potentially significant radiomic features based on the Spearman correlation coefficient. A 10-fold cross-validation with 500 bootstrapping repetitions was performed to minimize bias and overfitting. Three and 5 features were used for OS and LPFS prediction, respectively. Three models, namely clinical, radiomic and clinical-radiomic models were built including. For each model, C-index and respective CIs were obtained from the bootstrap estimate. The likelihood-ratio test was used to compare the performances of the models, with a p-value<0.05 indicating that radiomics led to an improvement in predictivity.

Results: One-hundred five predominately male pts were included in the analysis. Median age was 59 (IQR: 52-66) years, and stage IVA was the most represented (70%). HPV status was positive in 63 cases, negative in 7 and missing in 35 patients. Median follow-up was 6.3 (IQR: 5.5-7.9) years. The RS could successfully stratify pts according to both OS (p<0.0001) and LPFS (0.0002) (Figure 1). The clinical-radiomic model yielded the best predictive performances as compared to the models implementing either clinical-only and radiomic-only information (C-index: 0.82 [CI: 0.80-0.84] for OS and 0.86 [CI: 0.86-0.89] for LPFS).

Conclusions: Our results show that radiomics could

bring clinically significant informative content in this scenario. The best performances were obtained by combining clinical and quantitative imaging variables, thus suggesting the potentials of complex modeling for outcome predictions in OPC patients treated with IMRT.

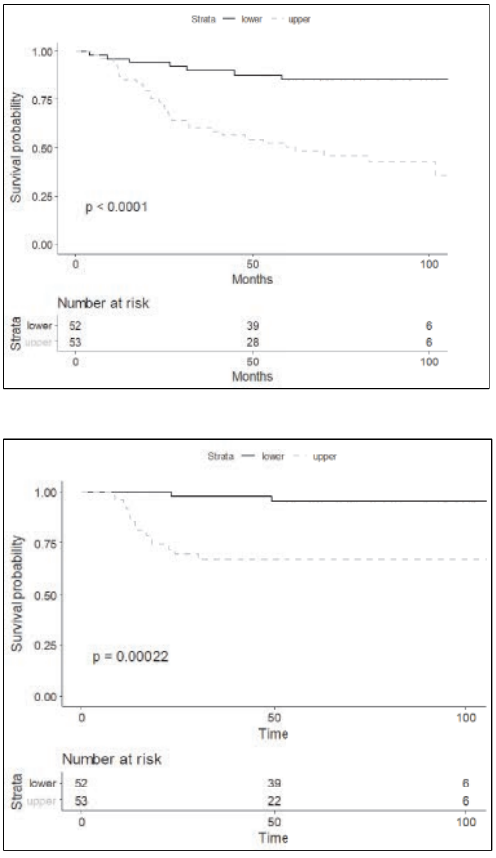

Figure 1. Overall Survival (OS) and Local Progression Free Survival (LPFS) per the radiomic score (RS).

CO31

UPFRONT ADVANCED RADIOTHERAPY AND NEW DRUGS FOR ADVANCED NSCLC PATIENTS WITH SYNCHRONOUS BRAIN METASTASES: IS THE JUICE WORTH THE SQUEEZE? A REAL-WORLD ANALYSIS FROM LOMBARDY

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Aims: Healthcare administrative databases represent a valuable source for real-life data analysis. Primary aim of this study is to compare effectiveness and cost profile in non-small cell lung cancer (NSCLC) patients harboring synchronous brain metastases who received non-chemo first-line systemic therapy with or without advanced radiotherapy.

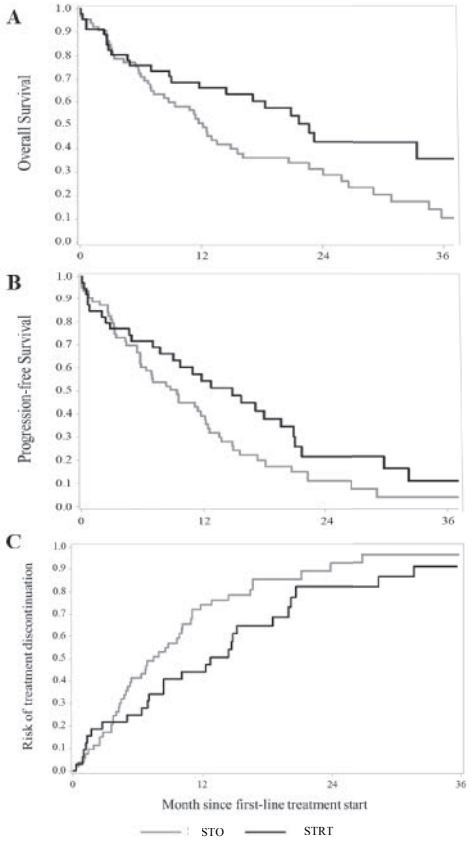

Figure 1. Kaplan-Meier estimates of overall survival (a), progression-free survival (b) and time-to-treatment failure (c) among patients with advanced NSCLC and synchronous brain metastasis treated with systemic therapy and advanced radiotherapy (STRT) or with systemic therapy only (STO). Footnote: in order to avoid immortal-time bias, in this analysis were only included patients who survived to the first three months of follow-up. For each patient, follow-up starts three months after the start of first-line systemic therapy.

Methods: Diagnostic ICD-9-CM codes were used for identifying all patients with a new diagnosis of lung cancer between 2012 and 2019. Among these, patients who had started a first-line systemic treatment with either TKIs or pembrolizumab for advanced NSCLC alone or in combination with intensity modulated or stereotactic radiotherapy were selected. Patients were followed from the date of first-line treatment start until 31st December 2020. Clinical outcomes investigated included overall survival (OS), progression-free survival (PFS), and time-to-treatment failure (TTF). The cost outcome was defined as the average per capita cumulative healthcare direct

costs for the treatment of patients included in the study cohort, including all inpatient and outpatient costs. Clinical outcomes of interest were estimated using Kaplan-Meier estimator and cumulative healthcare costs by treatment type were calculated using the Bang and Tsiatis estimator.

Results: The final cohort included 177 patients, of whom 58 were treated with systemic treatment plus advanced radiotherapy and 119 with systemic treatment alone. The addition of advanced radiotherapy to systemic treatment was associated with a significantly better OS (p=.020) and PFS (p=.041), than systemic therapy alone, while differences in the TTF resulted not significant (Figure 1). The ICER (incremental cost-effectiveness ratio) value indicated an average cost of 3,792 € for each month of survival after STRT treatment and confirmed clinical effectiveness (i.e., longer survival for patients on STRT therapy than systemic therapy alone), but higher healthcare costs.

Conclusions: This real-world study suggests that upfront advanced radiotherapy for NCLSC patients with synchronous brain metastases represents a valid treatment strategy, boosting the efficacy of novel and emerging drug classes with sustainable costs for the Health Service. These results warrant for further studies to identify the best radiotherapy timing and possible dose escalation approaches to improving treatment efficacy in patient subgroups not typically represented in randomized controlled trials.

CO32

PROCESS MINING: A NEW APPROACH FOR IMPROVING PATIENTS' CARE PATH IN HIGH VOLUME RADIATION ONCOLOGY DEPARTMENT

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Aims: Process mining is a machine learning-based methodology which can help clinicians to discover, monitor and improve processes by exploiting the daily collected real-world data for accurate and efficient workflow prototyping and visualization. The aim of this work is to perform a process mining - machine learning based analysis of the major events involving patients' path of cure in a high-flow Radiation Oncology department.

Methods: All patients treated from 2017 to 2021 in our department have been enrolled in the study. An analysis of the main events representative of the care path has been performed. Main events included are: first consultation, dose prescription, CT simulation, plan contouring, start and end of the treatment. Treatment suspensions/cancellation have been analyzed by categorizing underlying causes. A custom script has been developed to refine and convert data coming from our institutional database to event log template. Process mining analysis is expected to be performed by pMineR v.045b.

Results: More than 10,000 patients, that gave informed consent, were included and more than 100,000 events were considered in the study. Our data refining framework involved data collection and a preliminary analysis for event logs consolidation. The former step involved patient's age, site of tumor, prescribed dose, dates of the main events, linear accelerator, priority of the treatment. Cause of suspension/cancellation of the treatment were collected for patients undergoing these events. Later, the events and the attributes have been converted in an event log template suitable for machine learning analysis. The results of the preliminary analysis have showed that the 1 out of 5 radiotherapy treatment candidates has undergone treatment suspension/cancellation. Among the most common categories we found logistic issues and clinical impairments, both accounting for more than 20% of the involved cases. Among logistic issues, the most common causes were the rescheduling of the treatment due to machine ordinary and extraordinary maintenance, while among the clinical causes, 1 out of 3 patients had tumor-related complications (e.g. chemotherapy schedule not ended, etc.).

Conclusions: Our work clearly demonstrates the concrete role of process mining in allowing clinicians in gaining more awareness on the actual workflow to apply mitigation strategies and optimize patients' care path.

CO33

CORRELATION BETWEEN RADIATION DOSE TO BONE MARROW SUBREGIONS AND ACUTE HEMATOLOGIC TOXICITY IN ENDOMETRIAL CANCER TREATED WITH EXTERNAL BEAM RADIOTHERAPY

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Aims: To identify dosimetric parameters associated with acute hematologic toxicity (HT) in endometrial cancer treated with volumetric modulated arc therapy (VMAT-RT).

Method: Patients with uterine adenocarcinoma treated

in our Institution from March 2019 to Novembre 2021 were retrospectively enrolled in this study. All patients underwent adjuvant external beam radiotherapy with Volumetric modulated arc therapy (VAMT) strategy plus a brachytherapy boost on vaginal cuff. When indicated, adjuvant platin-based chemotherapy was administered after surgery in upfront or sandwich setting. Pelvic bone marrow was contoured for each patient and divided into three subsites: lumbosacral spine (LSBM), ilium (IBM) and lower pelvis (LPBM). The volume of each region receiving 10,20,30 and 40 Gy (V10, V20, V30, V40, respectively) and Dmean was collected. Hematological toxicity during radiotherapy treatment was graded according to the CTCAE V 5.0. Regression models were used to test associations between dosimetric parameters and HT.

Results: Data from 74 patients were retrospectively analyzed. Adjuvant external beam radiotherapy was delivered to the pelvis with Volumetric modulated arc therapy (VAMT) strategy for a total dose of 45 Gy, 1.8 Gy/fraction plus a brachytherapy boost on vaginal cuff for a total dose of 10Gy in 2 fractions weekly. Thirty-one patients developed during radiotherapy treatment an HT > grade 2. With a sensibility of 68.7% and specificity of 57.1%, V20 Gy of LSBM > 96% is associated with an increased Grade 2 or worse HT (95% Confidence Interval 0.50-0.74; p=0.049). No association between hematological toxicity and V10-20-30-40 or Dmean of IBM and LPBM were observed. Dosimetric parameters involving the lower pelvis had stronger association with hematological toxicity than those involving the ilium, even if not significant.

Conclusions: The volume of lombo-sacral pelvis receiving low-dose radiation (V20 LSBM >96%) seems to be associated with HT. Future investigations should seek to confirm these findings through the inclusion of these parameters in the planning process.

CO34

INTRA-OPERATIVE RADIATION (IORT) AT THE TIME OF PELVIC SALVAGE EXENTERATION IN PERSISTENT OR RECURRENT GYNECOLOGIC MALIGNANCIES: A SERIES OF 55 PATIENTS

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Aims: Intraoperative radiotherapy (IORT) is a modality that allows for an additional high, single radiation dose to be delivered safely while minimizing the dose to adjacent normal tissues. For this reason, IORT is well suited as an adjunct to tumor resection in patients with persistent or recurrent gynecologic malignancies undergoing salvage pelvic exenteration (PE). The present study aimed to review our experience using IORT at the time of PE, in terms of disease free survival (DFS) and overall survival (OS).

Materials and Method: We conducted a retrospective monocentric study from January 2001 to March 2019. Inclusion criteria were the following: 1) patients with a diagnosis of persistent or recurrent, previously heavily treated, gynecologic malignancies who underwent planned PE with curative intent; 2) all gynecologic cancers were considered; 3) IORT administration planned for not radical surgical margin (SM), positive lymph nodes or microscopic disease extended to <1 mm of the resection SM.

Results: Overall 55 patients matched inclusion criteria. Baseline characteristics are summarized in Table 1.

Table 1. Patients' Characteristics (N=55).

Variable	median	range
Age (years)	54	23-76
	N	**%**
Type of tumor		
cervical	40	72.7
vulvar	3	5.5
vaginal	6	10.9
endometrial	6	10.9
Previous oncologic treatment	53	96.4
Radiotherapy alone *	10	
Brachytherapy alone followed by chemotherapy	1	
Radiotherapy + brachytherapy¥	10	
Chemoradiation	12	
Chemoradiation + Brachytherapy	20	
Reason for surgery		
persistent disease	24	43.6
recurrent disease	31	56.4
Type of exenteration		
total	35	63.6
anterior	18	32.7
posterior	2	3.6
Margins		
positive	19	34.5
negative	36	65.5
Pelvic lymph nodes (surgically assessed)	37	67.3
positive	12	32.4
negative	25	67.6
IORT		
monolateral	46	83.6
bilateral	9	16.4
Field of irradiation*		
right pelvic wall	25	39.1
left pelvic wall	34	53.1
pubic symphysis	4	6.2
sacrum	1	1.6
IORT dose (median, range), Gy	15 (10-20)	
IORT energy (median range), MeV	6 (3-9)	
Diameter of the applicator (median, range), cm	5 (4-8)	
Depth of irradiation (median, range), cm	0.5 (0-8)	

IORT was delivered because of positive lymph nodes in 12 cases, of positive SM in 19 cases and in 24 patients because microscopic disease extended to <1 mm of the resection margins. The median follow-up was 35 months (range, 3-152 months). Overall 3-year DFS was 34.7% (median 11.8 months, 95% CI 6.1-17.6) and 3-year OS was 41.8% (median 24 months, 95% CI 14.5-33.5). SM were classified as negative (36 of 55, 65.5 %) or positive (19 of 55,34.5%). The 3-year local control rate was 64.4% in patients with negative SM compared to 45.7% in patients with positive SM (P=0.6). 23 patients relapsed (57.5%), 18 of those in the IORT field. The identified risk

factors associated with high risk of recurrence in field of IORT were cervical cancer (HR 10.3, 95% CI 1.2-86.5, P=0.03) and Grade 3 histology (HR 10, 95% CI 1.1-95.2, P=0.04). We also observed a trend in the correlation between positive SM and risk of recurrence in IORT field.

Conclusions: Survival in patients with high risk to have positive margin at final pathology after radical surgery alone showing particularly dismal survival rates. IORT is a viable option during salvage PE for recurrent or persistent gynecologic cancer still, with limited data, that might be considered to consolidate areas at high risk of relapse due to close or microscopically positive margins. In some selected patients, long term tumor control can be obtained. Whether IORT can improve local recurrence rates will require further prospective investigation.

CO35

A COMPREHENSIVE MULTIVARIATE ANALYSIS OF MULTIPLE SYSTEMIC INFLAMMATION MARKERS IN CERVICAL CANCERS UNDERGOING DEFINITIVE CHEMORADIATION

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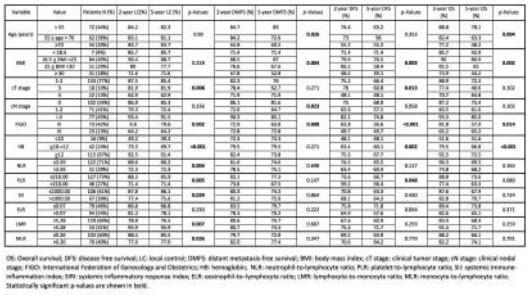
Aims: Interest in radiotherapy (RT) about markers of systemic inflammation has spread due to their value in predicting outcomes in several tumors treated with RT. However, only few data are available on the impact of these markers in locally advanced cervical cancer (LACC) patients (pts). Moreover, in most studies, only one index with only a partial consideration of potential confounding factors was evaluated. Therefore, the aim of this study was to analyze a wide range of inflammation indices by including also other known prognostic factors.

Method: We retrospectively analyzed pts undergoing chemoradiation (ChRT) for LACC from July 2007 to July 2021. Pretreatment values of several indices were calculated: neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), lymphocyte to monocyte ratio (LMR), monocyte to lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), and eosinophil to lymphocyte ratio (ELR). An univariate analysis (logrank test) on the impact of individual parameters on local control (LC), distant metastasis free survival (DMFS), disease free survival (DFS), and overall survival (OS), was performed. Furthermore, a multivariate Cox analysis on the same endpoints was performed including parameters significantly correlated with outcomes at univariate analysis.

Results: One hundred and seventy three patients were included in this analysis. The results of the univariate analysis are shown in Table 1. On univariate analysis no index of systemic inflammation was significantly correlated with DMFS, DFS, and OS, while a significant correlation with better OS rates was observed for patients with physiological BMI values, with less advanced FIGO stage, and with higher hemoglobin levels. Instead, on univariate analysis, NLR, PLR, SII, LMR, and MLR were significantly correlated to LC. However, on multivariate analysis, higher LC rates were significantly correlated only to higher hemoglobin levels (HR 0.57; 95% CI: 0.46-0.71, p<0.001).

Conclusions: Our study suggests a limited role of systemic inflammation markers in predicting prognosis in LACC pts undergoing ChRT, while confirming the dramatically negative impact of anemia in this setting. However, further studies are underway to evaluate: i) the impact of inflammation markers assessed after ChRT; ii) the possible correlation between inflammation markers and sarcopenia and the predictive role of their combination in this setting.

Table 1.



CO36

LADIES PROJECT: LARGE DATABASE IN ENDOMETRIAL CANCER FOR A PERSONALIZED TREATMENT

R. Autorino[1], R.M. Rinaldi[1], V. Vavassori[2], S. Lucci[1], G. Macchia[3], M. Boccardi[3], I. Mihoci Roshanian[4], R. Sebastiani[4], B. Santo[5], D. Russo[5], M. Ferioli[6], A. Benini[7], E. Perrucci[8], A. Raguso[9], S. Cossa[9], P. Matteucci[10], C. Talocco[10], F. Trippa[11], L. Draghini[11], A. Augurio[12], F.C. Di Guglielmo[12], P. Cocuzza[13], L. Vicenzi[14], F. Pistis[15], F. De Felice[16], M.A. Gambacorta[1], C. Aristei[8]

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Aim: With the aim to create predictive models of toxicity and survival for endometrial cancer, a retrospective-prospective multicentric Italian study was designed.

Method: A large database was built in 6 months by 3 of the authors and then shared with other 5 collegues to create a project's core group. A protocol for the restrospective and prospective study was designed and approved by the coordinator centre ethical committee and by the single participating centres ethical commitee. So far, 37 centres asked to participate in the study. This preliminary first analysis referes to one thousand six hundred seventy-seven endometrial cancer patients.

Results: Patients were treated between 2010 and 2020 with surgery, post-operative external beam radiotherapy and/or brachytherapy preceded or not by adjuvant chemotherapy, which was delivered on the basis of histological risk factors. A minimum of 12 months follow-up was required. Patients were enrolled in 14 Italian Radiation Oncology Centres (1 was in the North Italy, 12 in the Center and Isles, 1in the South) . Each centre enrolled a mean of 108 patients (range 390 – 14). Stages were from IA to IIIC. To develop predictive models, a comprehensive analysis based on clinical, radiological, and surgical findings, adjuvant therapies and outcomes will be performed.

Conclusions: We create a large database based on the Italian data in the management of endometrial cancer in Radiation Oncology Centres. Other than to allow a picture of the real word use of adjuvant radio- and systemic therapy for endometrial cancer, data will be used to develop clinical predictive models for personalization of endometrial cancer therapies.

CO37

INTRABEAM IN PELVIC CANCER: SAFETY AND FEASIBILITY

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Aim: Intraoperative radiotherapy (IORT) allows to deliver high doses of radiations to a well-defined target at the time of surgery, minimizing exposure to nearby organs at risk. The present retrospective single center study aims to evaluate treatment outcomes and reported toxicities in a cohort of pelvic cancer patients treated with IORT.

Materials and Method: Patients with pelvic disease treated between May 2019 and March 2022 were considered for study inclusion. Patients with high risk of positive margins received a IORT boost with a 50 kV X-ray source using the Intrabeam® RT delivery system to close or positive margins at the time of surgery. All patients signed a written informed consent to research purpose. Local and distant relapses and survival (OS) were analyzed. Acute and late toxicities were graded according to CTCAE 5.0 and RTOG criteria.

Results: A total of 18 consecutive patients and 22 lesions were treated. All patients were previously irradiated except one. Relapses were distributed as follows: 8 cervical, 2 vulvar, 2 vaginal, 4 rectal, 2 pelvic lymph-nodes. Flat applicators were used in 2 patients while surface ones for the others. Employed applicators had a diameter between 3 and 5 cm. Administered doses were: 6 Gy at 3 mm (9 Gy at surface), 8 Gy at 1 mm (11.4 Gy at surface), 9 Gy at 1mm (12 Gy at surface), 10 Gy at 1mm (13 Gy at surface), 9,5 Gy at 1 mm (14 Gy at surface), 12 Gy at 1 mm (16 Gy at surface) and 15 Gy at 1 mm (20 Gy at surface). At definitive histological report, 6 patients had 1-2 mm of free margins while 3 received adjuvant chemotherapy and 1 external beam RT. At time of analysis, 6 patients had no evidence of disease, 7 experienced distant metastases, 3 were lost at follow-up and for 2 had less than 6 months of follow-up. None of the post-surgical complications were correlated to IORT sites.

Conclusions: Preliminary evidence from our study suggest that INTRABEAM is a feasible and manageable IORT device in pelvic disease. More and updated data are needed in order to draw robust conclusions.

CO38

STEREOTACTIC RADIOTHERAPY BOOST IN LOCALLY ADVANCED CERVICAL CARCINOMA PATIENTS (STARBACS): UP-TO-DATE RESULTS OF A PHASE II, SINGLE ARM, MONOISTITUTIONAL STUDY

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Aims: To evaluate feasibility, toxicities and clinical outcomes (Local Control and Local Failure) in locally advanced cervical cancer patients treated with platinum-based chemotherapy concomitant to radiotherapy followed by SBRT-boost.

Methods: From February 2021 to June 2022 we enrolled all patients with a diagnosis of locally advanced cervical cancer (LACC), assigned to platinum-based chemo-radiotherapy (CT-RT), and unfit to brachytherapy, were submitted to IGRT Stereotactic Boost using a LINAC with six degrees of freedom table or a Robotic Arm LINAC.

Results: Eight patients with LACC (M0) have been enrolled. At the time of primary diagnosis all patients were FIGO-stage from IIb to IIIC1. Median age was 51 years (range 32-72); 7/8 had histological diagnosis of squamous-cell carcinoma HPV-related and 1/8 was adenocarcinoma. During concomitant treatment all patients received weekly Platinum-based chemotherapy (40 mg/mq) plus radiotherapy to a total dose on clinical target volume (CTV) of 46Gy (2 Gy/fx). All patients were submitted to SBRT-boost with a median total dose delivered of 21 Gy/3Fx (range 12-24Gy) on gross tumour volume (GTV) after restaging with contrast-enhanced MRI, 18F-FDG-PET, and Gold Fiducial implant. An isotropic margin of 2mm (PTV1-2) both on CTV and GTV has been applied. To contour we matched simulation-CT with contrast-enhanced MRI using the software MIM for deformable imaging fusion. Toxicities data registered were low: 62% dysuria G2, 50% fatigue G2 and one patient had nausea G2 and vaginitis G2. None of the patients showed toxicities ≥ G3. The median follow-up was 11 months (range 4-18) and local control has been obtained in 87.5% of the cases. One of eight patients showed local failure and underwent radical surgery.

Conclusions: These preliminary results showed that our approach with SBRT consolidation boost was feasible and well tolerated with encouraging results in terms of local control. Our data seem to indicate that this kind of therapy could emerge as a valid therapeutic option in LACC patients who cannot be submit to endocavitary brachytherapy.

CO39

IMAGE GUIDED BRACHYTHERAPY AND IMPLEMENTATION OF THE INTERSTITIAL TECHNIQUE IN LOCALLY ADVANCED CERVICAL CANCER

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Aims: The standard of care for women diagnosed with Federation of Gynecology and Obstetrics stage IB2 to IVA cervical cancer (locally advanced cervical cancer- LACC) is concurrent chemoradiation followed by intracavitary brachytherapy (BT). Supplemental interstitial catheters may be added in order to cover the maximum extent of gross residual disease (interstitial brachytherapy, HBT). The incorporation of magnetic resonance imaging in BT (Image Guided Adaptive Brachytherapy, IGABT) has increased the use of HBT in order to create a comprehensive treatment plan that covers the visualized tumor.

Method: Between January 2018 and December 2021, 199 patients with LACC were treated with primary radiation therapy including HBT. At the time of IGABT, the majority of women had a decrease in gross tumor size from 50.4 cc to 35.7 cc. Interstitial needles, with the use of an intracavitary tandem, has been selected for patients with large cervical lesions and/or lower vaginal involvement. A preliminary plan helped determine where to insert needles to increase the delivered dose.

Results: In the 199 patients, a total of 366 interstitial needles were implanted. Median follow-up was 19.2 months (range 6 – 41.4). Progression free survival and local control rate were 54.4, and 80.2%, respectively. Fifteen patients experienced local recurrence (7%). Of those, nine were confined to the uterus and six at the parametria. Acute adverse event ≥ grade 2 were seen in 23 patients; late adverse events ≥ grade 2 were seen in 17 patients.

Conclusions: The precision availed by MR-guided brachytherapy results in substantial improvements in needle positioning, and resulting treatment plans. Hybrid brachytherapy can be performed safely and with a high quality of radiation dose distribution.

CO40

STEREOTACTIC BODY RADIOTHERAPY IN OVARIAN CANCER PATIENTS PROGRESSING WITHIN PARP-INHIBITOR MAINTENANCE REGIMEN: ADVERSE EVENTS AND ACTIVITY FROM THE RETROSPECTIVE "EPIMETHEO" STUDY

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Aims: The benefit of surgery and maintenance treatment with Poly (ADP-ribose) polymerase inhibitors (PARPi) has been recently shown in ovarian cancer (OC) recurrence. The management of oligometastatic progression (OMP) during PARPi maintenance is unclear and continuing the treatment beyond progression could be an option. Furthermore, the efficacy and safety of stereotactic body radiation (SBRT) in patients with metastatic, persistent, and recurrent OC are proven. The aim of this observational, retrospective, multicenter study (Epimetheo) was to define the activity and safety of the SBRT in a real-world data set of patients with OMP during PARPi maintenance.

Methods: Patients treated with PARPi in maintenance setting received SBRT if OMP occurred. OMP was assessed by either Computed Tomography (CT)-scan or PET/CT scan, and in the case of < 5 lesions, SBRT was prescribed. Maintenance treatment was continued until the extensive progression of the disease. The endpoints of the study were the rate of complete response (CR) to SBRT plus concomitant PARPi therapy and acute toxicity profile assessment. The objective response rate (ORR) included CR and partial response (PR). Toxicity was evaluated by the Common Terminology Criteria for Adverse Events (CTCAE) scale.

Results: From May 2019 to January 2022, SBRT was used to treat 56 OC patients with a total of 107 lesions (69 lymph nodes and 38 parenchymal lesions) under PARPi maintenance. The patient characteristics and some treatment details are shown in Table 1. Olaparib, Niraparib, and Rucaparib were administered to 46%, 45%, and 9% of patients, respectively. Treatment response was assessable in 103 lesions with a median time to the best response of 5 months (1-14 months): CR, PR, and stable disease were observed in 62 (61%), 32 (31%), and 7 (7%) lesions respectively. Two lesions (2%) progressed. Out of 63 adverse effects, 56 were Grade 1, five were Grade 2, and two were Grade 3. Both severe acute toxicities (pain flare and upper gastrointestinal toxicity) occurred in the same patient who was treated for a retro-esophageal lymph node recurrence with 35 Gy in 5 fractions.

Conclusions: This study confirms the activity and safety of SBRT in patients in association with PARPi in this clinical setting. The toxicity rate in this series is consistent with that described in the literature on the stereotactic technique, and the addition of the PARP inhibitor did not worsen the toxicity.

Table 1. Patients 'characteristics and treatment details.

	N. (%)
All	56
Age, years	
Median (range)	57 (33-79)
BRCA gene status	
Wild type	3 (5.3)
Mutated BRCA1	25 (44.6)
Mutated BRCA2	23 (41.1)
Mutation Not specified	4 (7.1)
Not Available	2 (3.5)
Histotype	
High grade serous	52 (92.8)
Endometrioid	3 (5.3)
Carcinosarcoma	1 (1.8)
Previous Lines of Chemotherapy	
1	10 (17.8)
2	28 (50.0)
3	11 (19.7)
4-5	6 (10.7)
Not Available	1 (1.8)
PARP inhibitors regimen	
Olaparib	26 (46.4)
Niraparib	25 (44.7)
Rucaparib	5 (8.9)
Type of lesion(s)	
Lymph node	69 (64.5)
Parenchyma	38 (35.5)
Anatomical district	
Abdomen	53 (49.5)
Thorax	32 (29.9)
Brain	11 (10.3)
Pelvis	9 (8.4)
Neck	2 (1.9)
Median GTV (range), cm3	12.99 (0.01-22.98)
Median PTV (range), cm3	32.12 (0.34-53.64)
Median dose/fraction, (range), Gy	40/8, (25.5-50)
Median BED$_{\alpha/\beta 10}$ (range)	72 (38.25-105.6)

CO41

ABSTRACT NOT PUBLISHABLE

CO42

SURVIVAL OUTCOMES FOLLOWING INTERNAL MAMMARY NODE IRRADIATION IN LOCALLY ADVANCED BREAST CANCER

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Aims: The routinary inclusion of internal mammary

lymph node irradiation (IMLN RT) in the traditional nodal targets in patients (pts) affected by locally advanced breast cancer (LABC) is still a matter of debate. Literature reported different and controversial results regarding the balance between the improved outcomes and acceptable toxicities. That's why the aim of our study was to retrospectively, evaluate the outcome and major toxicities related to the irradiation of IMLN.

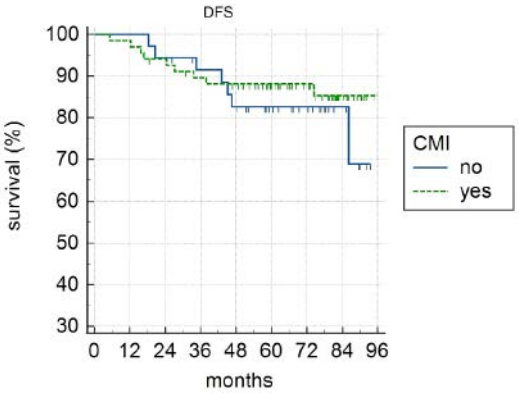

Figure 1.

Method: We retrospectively analyzed 105 pts affected by LABC, staging IIB-IIIC according to TNM 7th edition, from February 2013 to November 2017. Median age was 54 (range 32-80). Infiltrative ductal carcinoma histology was evidenced in most of pts (82%). Most of pts had a 3 tumor grading (G3) (55%) and 12% had triple negative receptor status. Eighty-two pts (78%) underwent mastectomy and 22% conservative surgery, followed respectively by conventional 3D conformal RT at the level of thoracic wall (50 Gy) and at the level of whole breast (50 Gy) with a boost of 10 Gy on surgical bed. All pts underwent RT at the level of regional lymph nodes: 65% underwent IMLN-RT. Comparison between two groups, one with pts who underwent IMLN RT and one with pts who did not, was performed in terms of disease-free survival (DFS) and overall survival (OS) as main outcomes and acute and late toxicity. Kaplan-Meier analysis and log-rank test, with p value significance <0.05, were used for statistical analysis.

Results: Median follow up was 65 months (3-95 mos). Ten pts (9%) developed distant metastases, 2 pts at the level of IMLN. After 5 years we didn't evidence statistically significant differences between the two groups in terms of DFS (p=0.44; 88.1% of DFS with IMLN RT and 82.6% of DFS without IMLN RT) and OS (p=0.28; 90.8% with IMLN RT and 83.4% without IMLN RT). Acceptable lung and heart toxicities were evidenced also in pts who underwent IMLN RT.

Conclusions: Our data, as well as other studies in the literature, didn't find improved survival with the irradiation of IMLN. A partial but not statistically significant advantage with IMLN RT was observed. A more numerous sample of pts and a longer follow up is needed in order to assess the real effectiveness of IMLN RT and to select the subgroup of pts who may benefit from irradiation of IMLN.

CO43

SIMULTANEOUS INTEGRATED BOOST (SIB) INTENSITY-MODULATED RADIOTHERAPY FOR TREATMENT OF BONE METASTASES: ANALYSIS OF A BREAST CANCER COHORT

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Aims: Bone metastases have an incidence of up to 75% in metastatic breast cancer, thanks to the evolution of imaging we can identify them in the oligometastatic phase. With the introduction of target therapies and increasingly effective conjugated antibodies, it is increasingly common to have to treat patients with radiotherapy for single or ≤5 bone lesions. The choice of volumes and dose in this setting does not yet have a clear indication. Surely the clinical need is to administer on the macroscopically evident disease an ablative dose that favors the control of disease. Aim of this analysis is to evaluate the outcome of pts receiving SIB for treatment of bone metastases.

Methods: A retrospective analysis including mBC patients (pts) undergone RT on bone metastases was conducted between January 2014 and January 2022. Primary endpoints was freedom from local progression (FFLP). Rate of disease progression after radiotherapy (DP-AR) and overall survival (OS) were secondary endpoints. Subgroup analysis (age, immunophenotype, line of therapy) were performed.

Results: On 954 mBC who underwent radiotherapy on metastases, 85 pts underwent SIB-IMRT with a boost on macroscopic lesion of 8-6 Gy in 5 fr. Mean follow up was 41 months (6-61.5 m). Nineteen pts had single bone metastase (22.4%), 20 pts were oligometastatic (23,5%), 46 pts were plurimetastatic (54,1%). FFLP was 17

months (95% CI 3.2-61.5 m). Only 6 pts (7%) had local relapse. DP-AR was 13,2 m (95% CI 3.1-56.9 m). OS was 82,7 m (95% CI 10.6-343 m). Local-relapse was not associated with age, immunophenotype or sistemic line ongoing. Among secondary outcomes, DP-AR resulted associated to immunophenotype (p 0.002). DP-AR and OS were not significantly associated with local relapse (respectively p 0.148 and p 0.4).

Conclusions: Pts with breast tumor can be treated with SIB-IMRT on bone metastases with a 93% of local control at 17 months from radiotherapy. Further data are needed to individuate pts who can benefit of dose-escalation and also sinergic effect with systemic therapies to possibly increase DP-AR.

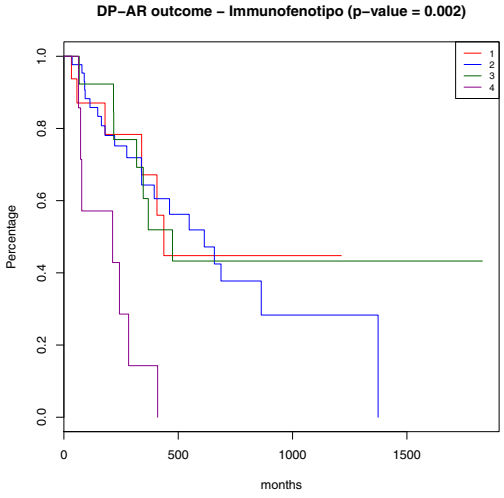

Figure 1.

CO44

POSTOPERATIVE RADIATION THERAPY IN BREAST CANCER BEARING PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY: A SINGLE INSTITUTION REPORT

M. Caroprese[1], E. Chioccola[1], S. Coppola[1], C.A. Goodyear[1], A. Barillaro[1], M. D'Arienzo[1], M. Petrazzuoli[1], A. Viggiano[1], S. Clemente[1], C. Oliviero[1], I. Lanzini[1], G. Arpino[2], M. Giuliano[2], C. De Angelis[1], V. Forestieri[1], A. Farella[1], R. Pacelli[1], M. Conson[1]

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Aims: Neoadjuvant chemotherapy (NAC) is commonly used for locally advanced and inflammatory breast cancer (BC) and, in the case of triple-negative and HER2-positive BC, in earlier stage. Achieving pathological complete response (pCR) after NAC predicts better outcome. The aim of this study was to investigate the patterns, timing, and risk factors for recurrence and survival outcomes in patients with BC treated with NAC, radical surgery and adjuvant RT.

Method: One hundred twenty-two patients treated with NAC, surgery, and adjuvant RT at our institute between April 2004 and May 2021 were enrolled. Medical records were reviewed for clinical stage, tumor grade and molecular subtype, NAC regimen, type of surgery, pathologic stage, recurrence, and death. pCR was defined as absence of residual invasive cancer on pathological evaluation of resected breast and all sampled lymph nodes after NAC.

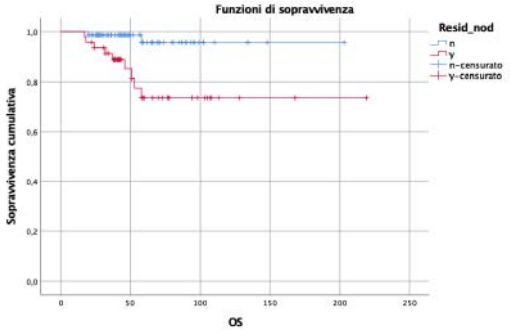

Figure 1. Five-year Overall Survival in the pN negative (blue) and pN positive (red) group.

Results: Fifty-two patients (42.6%) had clinical stage III BC, seventy (57.4%) stage II. According to molecular subtypes, luminal A accounted for 38 patients (31%), luminal B for 55 (45%), Her2-enriched for 14 (12%), triple negative for 15 (12%). Forty-one patients (33.6%) achieved pCR. At a median follow-up of 38 months (5-209), 11 patients (9%) were dead; 3 patients (2.5%) had locoregional recurrence only, 13 patients (10.7%) had distant metastasis only, while 4 patients (3.3%) had both locoregional recurrence and distant metastasis. Actuarial rates of LRRFS, PFS, and OS at 5 years were 94.2%, 84.2%, and 86.7%, respectively. Regarding pCR, no significant differences were seen in LRRRFS rates (p= 0.263), and PFS (p=0.650). Although 5-year OS rates were 83.6% in patients that did not achieve pCR and 92.9% in patients that achieved pCR, this expected difference resulted not significant (p=0.238). Among cN0 patients (18.9%), final node status was ypN0 in 95.7%. In cN1 patients, nodal pathologic complete response was 57.6%, and residual nodal disease included ypN1mi in 4%, ypN1 in 23.2%, ypN2 12.1%, and ypN3 3%. The 5-year OS in the pN negative and pN positive group were 95.7% and 73.6% (p=0.003), respectively (Figure 1). LRRFS and DFS were also significantly different between the two groups, with the ypN negative group

showing improved survival rates.

Conclusions: NAC, surgery and postoperative RT are an effective treatment in patients with high-risk BC. Residual nodal disease after NAC seems to be more important than residual breast burden as predictor of survival.

CO45

BRIDGING RADIOTHERAPY BEFORE CAR-T CELL INFUSION FOR DIFFUSE LARGE B CELL LYMPHOMA. THE EXPERIENCE OF SAN BORTOLO HOSPITAL (VICENZA)

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Aims: Complicating chimeric antigen receptor (CAR)T-cell therapy is a promising treatment for relapse/refractory aggressive B-cel lymphoma. Sometimes from the preparation of engineered T-cells to their infusion the disease may progress. Radiation therapy(RT) in alternative or concurrent to chemotherapy can be used as a bridging strategy. In this study our aim was to evaluate the feasibility and the effectiveness of bridging RT in absence of increased toxicity.

Method: We reviewed all the patients treated in our hospital with CAR-T cell infusion. All data were prospectively collected. We analyzed all treatment details, toxicity and disease course.

Results: All cases were reviewed by our hematological tumor board and the indications for RT were local and symptom control. In all cases RT was given after apheresis and some of the patients received their RT treatment in referring istitutions. Between May 2020 and April 2022 21 patients were treated in our hospital with CAR-T cell therapy. The whole group of patients was characterized by primary refractory diffuse large B cell lymphoma (DLBCL). 13 patients received TISA-CEL and 8 patients ACI-CEL therapy. All of the patients received a type of bridging therapy before the CAR-T cell infusion and 12 patients were intended to receive bridging radiation. All patients in the RT group received 2 to 10 Gy/fraction to a median total dose of 24 Gy(range 20-36 Gy). 8 patients received concurrent chemotherapy. After bridging RT 11 patients underwent CAR-T cell infusion and one did not. Median follow up was 7 months (range 1-20,7 months). There was non grade 3 o higher toxicity from RT and non unplanned delays in the CAR-T cell infusion due to RT. No patient experienced in-fied disease progression before infusion but 8 patients experienced out of fied disease progression. At 30 days the objective response rate was 72% with complete response in 44% of cases.

Conclusions: Bridging radiation therapy (with or without concurrent chemotherapy) can be safely administered prior to CAR-T cell infusion in high risk lymphoma. No grade 3 o higher RT toxicities occured in this series. Future investigation to prospectively define the optimal RT features (total dose, dose/fraction, timing) is needed.

CO46

EFFECT OF NUMBER OF ADMINISTERED LINES OF SYSTEMIC TREATMENT ON SYMPTOMATIC AND RADIOLOGIC RESPONSE TO RADIOTHERAPY OF MULTIPLE MYELOMA: A SUB-ANALYSIS OF RR-MYELO POINT RETROSPECTIVE STUDY

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Aims: Although multiple myeloma (MM) is higly chemo- and radio-sensitive, multiple mechanisms of treatment resistance almost invariably lead to treatment resistance and disease progression. As the impact of systemic treatment on radiosensitivity has not yet been clinically explored, we planned this study to provide real-world data on this topic.

Methods: In RR Myelo-POINT study we retrospectively analyzed the data from 312 patients (577 lesions) who received radiotherapy at our institution from 2005 to 2020. Data regarding clinical features, radiotherapy, systemic treatment and disease response were retrieved from the electronic medical record systems and picture archiving and communication system. Patients were divided in three groups according to the number of systemic treatment lines administered at the time of radiotherapy (no systemic treatment, 1-2 lines and 3 or more lines).

Results: Radiological response rate at six months (data available for 181 lesions) was 79%, with only 4.4% of lesions in progression with no effect of the number of systemic treatment lines (p=0.227); there were as well no statistically significant difference across the three different groups (p=0.078). Radiotherapy resulted in a pain control rate of 97% at one month after radiotherapy, that remained stable at three and six months (96.9% and 94%, respectively) with no significant difference between the three different groups (p=0.978 at one month, p=0.360 at three months and p=0.416 at six months)

Conclusions: The number of lines of systemic treatment administered had no statistically significant impact on symptomatic and radiologic response to radiotherapy, suggesting that MM retains its radiosensitivity also after multiple treatments.

CO47

MANAGEMENT OF CARDIAC IMPLANTABLE DEVICES DURING RADIATION THERAPY: A SINGLE CENTRE EXPERIENCE

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Aims: Over the past few years, an increasing number of cardiac implantable electronic devices (CIEDs), including both pacemakers (PM), implantable cardiac defibrillators (ICD) and loop recorders (LR), has been used to manage various type of cardiac arrhythmias. Considering that the number of radiation therapy (RT) treatments is increasing, to ensure a safe management of all the devices has become mandatory. The aim of this work is to explain how CIEDs are managed in a single centre experience.

Methods: We evaluated and described our activity from the end of June 2010 to September 2021; the clinical data was downloaded from a database including all the patients with CIEDs treated in our department.

Results: 215 patients with CIEDs were treated in our Institute in the period in analysis: 149 patients with PM, 65 with ICD and one with LR. 40 radiation treatments were re-irradiations. Beam energy for all the therapies was X6 MV; 68 patients were treated with 3D conformal RT, 30 with intensity-modulated RT, 116 with stereotactic RT and one with brachytherapy RT. In agreement with our Cardiologists, a procedure for this kind of patients has been designed by defining probability classes for the CIEDs damage risk. On the base of the assigned risk class (low, intermediate, or high) we differently monitored the patients during the radiation delivery: 33 patients in the low-risk class were audio-visual monitored by radiation oncologists; 148 patients in the intermediate risk class were monitored with electrocardiogram (ECG) and pulse oximeter by radiation oncologists and nurses; in 34 cases, representing the high-risk class, even the presence of a cardiologist was considered necessary. During the treatments any adverse event has been registered: one patient died due to other causes.

Conclusions: Our Institute CIEDs management is based on a multidisciplinary team and on the training of the RT staff. This method appears to be safe and permits the access to the RT to all the patients with CIEDs; however, further study is deemed useful to update the current knowledge to the quick progress in technologies.

CO48

A NEW INDEX FOR PAIN MANAGEMENT ASSESSMENT (MIAMI: MODIFIED PAIN MANAGEMENT INDEX) SHOWS THAT PATIENTS ARE REFERRED TOO LATE TO PALLIATIVE RADIOTHERAPY. A SUB-ANALYSIS ON 1042 PATIENTS FROM THE ARISE STUDY

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Aim: In the ARISE multicenter prospective observational study we evaluated the adequacy of pain management during radiotherapy (RT) using the Pain Management Index (PMI). However, the PMI has several limitations. In particular, in patients with severe pain despite the use of strong opioid drugs, the PMI is 0, improperly indicating the adequacy of therapy. Therefore we introduced a new index (MIAMI: ModifIed pAin Management Index) aimed at overcoming this PMI limitation. Moreover, we used the MIAMI to evaluate the adequacy and efficacy of analgesics prescribed to patients referred to RT.

Methods: Patients, tumors, drug therapy, and pain

characteristics were collected during the first visit in RT departments. A Pain Score was defined with values between 0 (no pain; NRS: 0) and 3 (severe pain; NRS: 7-10). An Analgesic Score was defined with values between 0 (no pain medication) and 3 (use of strong opioids). The PMI was calculated by subtracting the pain score from the analgesic score. All patients with PMI<0 or patients with PMI≥0 but with pain score>1 (NRS>4) were considered to have a negative MIAMI score (MIAMI-). On the contrary, all patients with PMI≥0 and pain score<2 (NRS≤4) were considered to have a positive MIAMI score (MIAMI+). Practically, if the PMI<0 includes only patients with inadequate analgesic therapy, the MIAMI includes both patients for whom analgesic therapy is inadequate and those for whom it is ineffective.

Results: One thousand forty-two patients were included. Fifty-eight percent of them complained of pain and were taking analgesic drugs. Patients were referred to curative and palliative RT in 75% and 25% of cases, respectively. Patients in curative RT showed PMI<0 and MIAMI- in 42% and 58% of cases, respectively, while in palliative RT the rates of PMI<0 and MIAMI- were 25% and 70%, respectively (Figure 1).

Conclusions: From our analysis the following conclusions can be drawn: (i) the higher rate of inadequate pain therapy in patients candidates for curative RT shows the lack of attention to this symptom in patients in better clinical condition; (ii) the very high rate of patients candidates for palliative RT with inadequate or ineffective pain therapy suggests that patients are referred to this treatment too late, when pain can no longer be controlled with drugs, but when the likelihood of achieving symptom relief with RT is clearly lower.

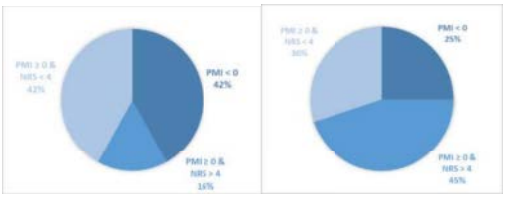

Figure 1. pie chart displaying the percentage of patients with PMI < 0 or PMI ≥ 0 and Numering Rating Scale (NRS) > 4 in patients undergoing curative (left) and palliative (right) radiotherapy.

CO49

CAN MR-GUIDED HIGH INTENSITY FOCUSED ULTRASOUND (MRGHIFU) REPLACE PALLIATIVE RADIOTHERAPY IN THE TREATMENT OF PAINFUL BONE METASTASES?

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Aim: External beam radiotherapy (EBRT) is a well-established treatment option in the treatment of pain from bone metastases. However, not all patients (pts) experience pain relief after EBRT. Moreover, it can take up to six weeks before adequate pain relief is reached and approximately 50% of initial responders experience recurrent pain. Magnetic Resonance image-guided High-Intensity Focused Ultrasound (MRgHIFU), as an alternative or in addition to EBRT, may improve pain palliation in these pts by increasing the percentage of responders and decreasing the time to response. However, large datasets on the feasibility of MRgHIFU are not available and therefore the rate of pts who can benefit from this therapy is unclear. Therefore, the purpose of this analysis is to report the preliminary results of pts screened in a radiotherapy center for inclusion in a randomized study of MRgHIFU versus EBRT versus MRgHIFU plus EBRT (The FURTHER-trial, H2020).

Methods: The inclusion criteria of the trial were as follows: painful metastatic bone lesion (NRS ≥ 4), pain from target lesion distinguishable from other lesions, target lesion location is accessible for MRgHIFU and EBRT, pts able to fit in the MRI gantry, reasonable performance score (KPS ≥ 50%). Exclusion criteria were as follows: neurological symptoms due to nerve involvement of target lesion, previous surgery or need for surgery of targeted location due to pathological fracture, unavoidable critical structures in the target area, curative intention of the treatment plan, contraindications for MRI or sedation.

Results: From February 2021 to June 2022, 153 pts were screened for inclusion and 151 (98.7%) were excluded from participating in the trial for the following reasons: spine or skull lesions (79 pts, 51.6%), NRS<4 or NRS=0 or non-distinguishable pain (30 pts, 19.6%), tar-

get lesion non-accessible for MRgHIFU or MRI contraindications (27 pts, 17.6%), previous surgery or pathological fractures (8 pts, 5.2%), KPS < 50% (4 pts, 2.6%), curative intent of EBRT(3 pts, 2.0%).

Conclusion: MRgHIFU is a promising modality of palliation in pain from bone metastases, especially in pts with symptoms resistant to EBRT. However, the results of our analysis show that the percentage of pts enrolled in a MRgHIFU trial is only 1.3%, with about 75% of pts excluded due to intrinsic limitations of this therapy. Therefore, the implementation of this technique could be justified only in a few centers with a high degree of expertise.

CO50

ESTABLISHING A BENCHMARK OF DIVERSITY, EQUITY, INCLUSION AND WORKFORCE ENGAGEMENT IN RADIATION ONCOLOGY IN EUROPE – AN ESTRO COLLABORATIVE PROJECT

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Background and purpose: Diversity, Equity and Inclusion (DEI) in the medical workforce is linked to improved patient care and innovation, as well as employee retention and engagement. The European Society for Radiotherapy and Oncology launched a survey to provide a benchmark of DEI and engagement among radiation oncology (RO) professionals in Europe.

Methods: An anonymous survey was disseminated among RO professionals in Europe. The survey collected demographics and professional information, and participants were asked if they felt they belonged to a minority group. A DEI and workforce engagement questionnaire by Person et al. evaluated 8 inclusion factors. A favourable score was calculated by adding the percentage of ''strongly agreed'' or ''agreed'' answers.

Results: A total of 812 complete responses were received from 35 European countries. 21% of respondents felt they belonged to a minority group, mostly based on race/ethnicity (5.9%), nationality (4.8%) and age (4.3%). Compared to benchmark data from the United States, scores were lower for most inclusion factors, and to a greater extent for minority groups. The overall favourable score was 58% for those belonging to a minority group, significantly lower than for other respondents (71%, $p < 0.001$). Those belonging to a minority group because of their gender or age had the lowest overall favourable score (47% and 51% respectively).

Conclusions: Our work indicates that actions to improve DEI and workforce engagement among RO professionals in Europe are urgently needed, in particular among minority groups. This would potentially improve employee wellbeing and retention, promoting high quality care and innovation.

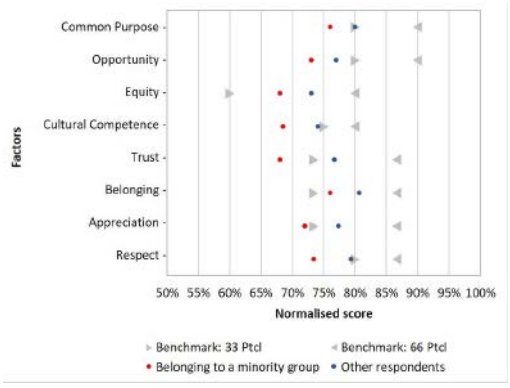

Figure 1.

CO51

SAFETY AND FEASIBILITY OF SBRT FOR THE MANAGEMENT OF ELDERLY AND FRAIL PATIENT WITH LOCALLY ADVANCED BLADDER CANCER

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Aims: To retrospectively describe the safety, feasibility and efficacy of stereotactic body radiotherapy (SBRT) for locally advanced bladder cancer (LABC) in a monocentric cohort of frail patients (pts) not eligible for radical cystectomy or systemic treatments (ST).

Methods: Pts not eligible for cystectomy and ST who underwent SBRT to the gross disease or to the tumor bed after transurethral resection of bladder tumor (TURBT) at

our Institution from 2017 to 2021 were considered for study inclusion. Photon SBRT was delivered with image-guided radiation therapy (IGRT) using three different linear accelerators. Schedules of treatment were of 30 and 25 Gy in 5 fractions (both every other day, and consecutive days). Treatment response was evaluated with radiological investigation and/or cystoscopy. Toxicity assessment was carried out according to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) v2.0 criteria.

Table 1. Summary of the patients' characteristics.

Group	Variable	Type	n (IQR, %)
SBRT post-TURBT (n=7)	*median age*	*years*	85.5 (IQR 83.6-87.6)
	gender	*male*	5 (71.4)
		female	2 (28.6)
	CCI	*7*	2 (28.6)
		8	2 (28.6)
		11	2 (28.6)
		12	1 (14.2)
	T stage	*p2*	2 (28.6)
		c2	2 (28.6)
		px	3 (42.8)
	N stage	*c0*	5 (71.4)
		c3	1 (14.3)
		cx	1 (14.3)
	M stage	*c0*	5 (71.4)
		c1a	2 (28.6)
	acute toxicity	*G0*	6 (85.7)
		G1	1 (14.3)
	chronic toxicity[6]	*G0*	5 (71.4)
		G1	1 (14.3)
SBRT only (n= 11)	*median age*	*years*	80.1 (IQR 73.6-82.4)
	gender	*male*	8 (72.2)
		female	3 (27.3)
	CCI	*6*	1 (9.1)
		7	2 (18.2)
		8	1 (9.1)
		9	4 (36.3)
		10	1 (9.1)
		11	1 (9.1)
		12	1 (9.1)
	T stage	*c1*	1 (9.1)
		c2	4 (36.4)
		c3b	2 (18.2)
		c4a	1 (9.1)
		cx	1 (9.1)
		p2	1 (9.1)
		p4a	1 (9.1)
	N stage	*c0*	8 (72.7)
		c1c	2 (18.2)
		c3	1 (9.1)
	M stage	*c0*	6 (54.5)
		c1	4 (36.4)
		cx	1 (9.1)
	acute toxicity	*G0*	6 (54.5)
		G1	1 (9.1)
		G2	3 (27.3)
		G3	1 (9.1)

Results: A total of 18 pts were included in the study, 11 of them received SBRT on the gross disease (SBRT only group) and 7 on the tumor bed after TURBT (SBRT post-TURBT group). Baseline characteristics of the pts are shown in Table 1. The treatment was overall well tolerated, with three grade (G) 2 and one G3 acute genitourinary toxicities reported and one G4 chronic toxicity in the SBRT only group, that needed permanent catheterization and then bilateral nephrostomy. In the TURBT group no G>1 toxicity was reported. Pts' response to treatment for pts with available follow-up (FU) was evaluated with cystoscopy in 6 pts and with a CT scan in 5 pts. In the SBRT only group, at a median FU of 12.5 months (IQR 7.2-25.3) 2 complete responses to the treatment were reported; as of today, 5 out of 11 pts are alive; among them 1 patient had a complete response and 4 were lost at FU. For the SBRT post-TURBT group, at a median FU of 10.0 months (IQR 5.8-16.6) 4 out of 7 pts are alive with two complete, 1 partial response and 1 patient lost at FU. Overall, only 1 patient in the SBRT only group experienced a progression of disease.

Conclusion: To the best of our knowledge, this is the first report of SBRT for LABC in a frail and elderly population. Our preliminary data demonstrate that the treatment is technically feasible, with an acceptable toxicity profile. Additional and updated FU data on toxicities and oncological outcomes could help to provide more solid indications in this underrepresented setting of pts.

CO52

PELVIS OR NOT PELVIS, THAT IS THE QUESTION: A RETROSPECTIVE ANALYSIS ON WHOLE PELVIS RADIOTHERAPY (WPRT) VERSUS PROSTATE-ONLY RADIOTHERAPY (PORT) IN HIGH AND VERY-HIGH RISK NON-METASTATIC PROSTATE CANCER

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Aims: The role of whole pelvis radiotherapy (WPRT) in the setting of high and very high risk non-metastatic prostate cancer (HR-nmPca) is still highly controversial. Several trials and meta-analyses have tried to clarify the benefit of WPRT and its implications in terms of toxicity, but solid data to support it are still lacking, especially following the spread of new imaging techniques such as PSMA PET which have improved early identification of nodal metastases. Hence the need to add new clinical data, even retrospectively, to compare the two treatment strategies: WPRT vs Prostate-only radiotherapy (PORT).

Method: Data of 205 HR-nmPca patients (cN0 and cM0 according to TNM staging) who underwent normofractionated or hypofractionated RT (IMRT/VMAT with daily IGRT) from January 2011 to December 2016 in 2 italian radiation oncology centres, were retrospectively analyzed. A propensity score match analysis was performed based on age, ISUP grade, PSA and androgen depri-

vation therapy (ADT) time, to reduce selection bias. In this way, 2 homogeneous groups were identified: a first group of 61 pts treated with PORT and a second group with as many pts treated with WPRT. The endpoints were biochemical relapse-free survival (BrFS), Time to mCRPC, overall survival (OS) and cancer specific survival (CSS). Survival analysis was performed using Kaplan-Meier curves and relative log-rank test.

Results: The median follow up was 5 years for the PORT group and 5.5 years in the WPRT group. Biochemical failure (BF) occurred in 16 pts in the PORT group and 10 in the WPRT group (p= 0.262). Only 1 patient among those treated with WPRT developed pelvic lymph node recurrence, while 5 cases were observed in PORT group (p= 0.094). Time to mCRPC was 45.2 months for PORT group and 43.6 for WPRT group (p= 0.538); OS was 103.7 months with PORT and 115.3 with WPRT (p= 0.084), while CSS was 111.9 and 117.5 months in the two groups (p= 0.995). Clinically significative acute and late toxicities (CTCAE grade>3) were seen in a low percentage of pts in both groups: <1% for acute GU and GI toxicity and <3.2% for late toxicity.

Conclusions: WPRT did not result into an increase in toxicity, but at the same time it did not improve survival, although the follow-up is still too short. Nodal Metastasis-directed therapy at the time of BF may represent a viable and effective therapeutic option. The integration of PSMA-PET in frontline staging could lead to more accurate treatment decisions.

CO53

INTRAOPERATIVE DEFINITIVE RADIOTHERAPY FOR EARLY BREAST CANCER: EVIDENCE FROM MONOISTITUTIONAL BREAST UNIT

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Introdiction: To evaluate the clinical response rate after an intraoperative radiotherapy (IORT) in early breast cancer treated with conservaty surgery.

Material and Method: Patients with early breast cancer after lumpectomy plus IORT were included. Inclusion criteria were: >60 years old, tumor size ≤ 2 cm (stage ACCJ 7th edition: T1), luminal A carcinoma (positive hormonal receptors, negative HER2, low Ki67 value), patological negative lymph nodes (pN0). Exclusion criteria was the lobular carcinoma histology. IORT was administered with a dedicated applicator with the delivery of 21 Gy at the applicator surface (treatments characteristics are showed in Table 1). Clinical and/or instrumental follow-up were performed 45 days after IORT, 6 months after the first medical check, and thereafter every 12 months.

Table 1. Treatments characteristics.

	n	%
Patients	162	100
Lumpectomy	162	100
IORT	162	100
Applicator (cm)		
Median	6	
Range	5-6	
Energy (mEv)		
Median	8	
Range	6-8	
Dose (Gy)	21	
Adjuvant therapy		
Ormonotherapy	97	60.9
Chemotherapy	0	0.0

Results: One hundred and sixty-two consecutive patients were included in this analysis (median follow-up: 54 months, range: 1-98 months). Post-IORT clinical and instrumental analyses showed an overall response rate in 96.9% of patients (CI 95%: 0.93 – 0.99%). Locoregional relapse occurred in 5 patients (3.1%), subsequently treated with mastectomy. No patient (0%) showed distant metastases. During follow-up, 13 patients (8.0%) died for comorbidity, no one due to breast cancer. After treatments, no patient (0%) showed radiation-related acute complications, only a small proportion of patients (14.8%) experienced peri-operative complications as wound dehiscence, wound infection, and bleeding with hematoma. Late G2-3 toxicity occured in 3.7% of patients (moderate/severe tissues fibrosis). No patient experienced G4 late toxicity.

Conclusions: Our data confirmed that IORT is a feasible and valid therapeutic option in low-risk breast cancer patients treated with lumpectomy. Locoregional control, overall survival rates, and patients compliance were in agreements with those reported in literature. These results encourage future prospective studies to validate this technique in the clinical routine.

CO54

SELECTION CRITERIA FOR STEREOTACTIC BODY RADIOTHERAPY OF SPINE METASTASES. DETERMINANTS OF RADIORESISTANCE AND PROGRESSION FREE SURVIVAL

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Aims: Stereotactic Body Radiotherapy (SBRT) is commonly used for treatment of uncomplicated spine metastases to palliate symptoms and prolong disease control. However, criteria for patient selection are not available. The aim of this study is to identify determinants of local failure and progression-free interval in patients underwent to SBRT for spinal metastases.

Methods: Data from consecutive patients treated with Cyberknife-based spine SBRT between January 2019 and March 2020 were retrospectively collected. Dose was expressed as Biological Effective Dose for α/β=10 (BED10). Kaplan-Meyer method was used to calculate Local Control (LC) and Disease Free Survival (DFS) from date of SBRT to event. Univariate (UVA) and Multivariate analysis (MVA) were performed using log-rank and Cox model, respectively.

Results: Sixty-two patients accounting for 70 spinal metastases were included. Median age was 66 (range 32-87) years. Metastatic disease at diagnosis was in 21 patients (34%): an active primary tumor was present in 17 patients (27%). Among treated sites, most represented primary malignancies were prostate (n=28, 40%) and breast (n=21, 30%). Dose regimens consisted of 25-30 Gy in 5 fractions and 21-30 Gy in 3 fractions in respectively 61 (87%) and 9 (13%) cases, resulting in a median BED of 43.2 (range 37.5-60) Gy10. Concurrent chemotherapy (including cytotoxic or targeted agents) was administered in 43% of cases (n=30). After a median follow up of 10 months (range 1-24 months), 9 local relapses and 40 distant progressions were observed. One year LC was 87% (Figure 1): no prostate primary tumor (p=0.003, Figure 2) and concurrent chemotherapy (p=0.006, Figure 3) were associated to poorer LC at UVA, and an independent correlation was confirmed at MVA (respectively p=0.017 and p=0.024). One-year DFS was 43% (Figure 4). UVA showed a correlation between impaired DFS and active primary tumor (p=0.003), metastatic dissemination at diagnosis (p=0.02) and nonprostate primary tumor (p=0.009), although only an active primary tumor site was independently associated to DFS at MVA (p=0.007, Figure 5). We reported a low rate of toxicity, only G2 acute pain or nausea were observed. No late toxicity, in particular no vertebral fracture, was reported.

Conclusions: Spine SBRT results in high LC rates and durable progression-free survival with low incidence of mild toxicity. Clinical nomograms based on patient-related characteristics may allow the selection of SBRT eligible patients.

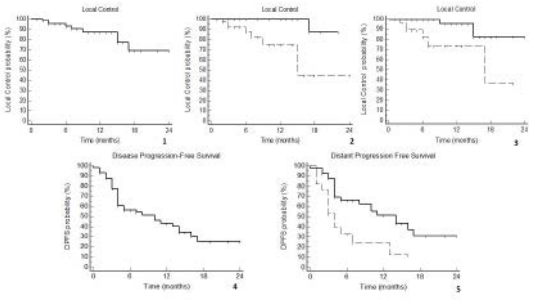

Figure 1.

CO55

SHORT COURSE PALLIATIVE RADIOTHERAPY IN ADVANCED SOLID TUMORS: A POOLED ANALYSIS (THE SHARON PROJECT)

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Background: Previous trials showed the tolerability and efficacy of a palliative radiotherapy (RT) regimen (SHARON) based on the 4 fractions delivered in 2 days in different oncological settings. In order to identify possible predictors of symptomatic response, the purpose of this study is to perform a pooled analysis of previous trials.

Material and Methods: We analyzed the impact on symptomatic response of the following parameters: tumor site, histological type, performance status (ECOG), dominant symptom, and RT dose using the chi-square test.

Results: One-hundred-eighty patients were analyzed. Median RT dose was 20 Gy (range: 14-20 Gy). The overall response rate was 88.8% (95%CI: 83.3%-92.7%) while pre- and post-treatment mean VAS was 5.3 and 2.5, respectively ($p < .001$). The overall response rate of pain, dyspnea, bleeding, dysphagia, and other symptoms was 86.2%, 90.9%, 100%, 87.5%, and 100%, respectively. Comparing the symptomatic effect based on the analyzed parameters no significant differences were recorded. However, patients with locally advanced disease showed a higher rate of symptomatic responses than metastatic ones (97.3% versus 83.0%; $p = .021$). Finally, the complete pain response rate was more than double in patients with mild to moderate (VAS: 4-7) compared to those with severe (VAS > 7) pain (36.0% versus 14.3%; $p = .028$).

Conclusions: This pooled analysis showed high efficacy of the SHARON regimen in the relief of several cancer-related symptoms. The markedly and significantly higher complete pain response rate, in patients with mild-moderate pain, suggests an earlier referral to palliative RT for patients with cancer-related pain.

CO56

RADIOMIC FEATURE RELEVANCE IN THE PREDICTION OF PATHOLOGICAL FEATURES OF PROSTATE CANCER

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Aims: The purpose of this study was to compare the contributions of radiomic signatures in the prediction of prostate cancer features with prostatectomy as confirmation.

Methods: A subset of 100 patients from the cohort of about 1500 who have undergone MRI and prostatectomy in our Institution since 2015 was selected by balancing the clinical characteristics of the patients. The prostate of each patient was segmented from T2-weighted axial MRI images by an expert radiologist, and 1810 radiomic features were extracted (PyRadiomics v3.0.1, AIM-Harvard). The radiomic feature set was reduced to 50 features using a hierarchical clustering procedure based on absolute rank correlation. In each cluster, the feature with the highest absolute rank correlation with the target variable was selected. Gradient-boosted decision-tree models were separately trained using clinical variables (age, prostate volume, iPSA, EPE score and PI-RADS category, biopsy-based total Gleason score and ISUP grade, and risk class) alone and in combination with the selected radiomic features to predict: surgical marginal status (R0 vs R1), pathology-based lymph node status (pN0 vs pN1), tumor stage (pT2 vs pT3) and ISUP grade group (<3 vs ≥4), and validated with repeated 5-fold cross validation. The mean feature importance in the clinical + radiomic feature models was determined based on mean prediction value change over validation folds.

Results: The validation AUC values (±95% CI) of the different models were 0.800 (±0.007) for surgical marginal status, 0.871 (±0.010) for pathological lymph nodes, 0.795 (±0.006) for pathological tumor stage, and 0.877 (±0.009) for ISUP grade group (Figure 1).

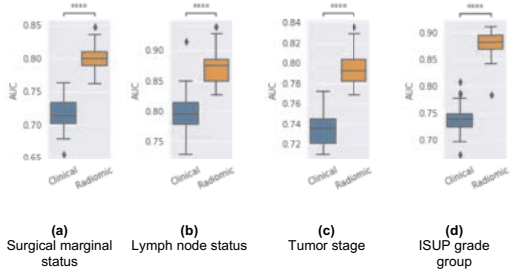

Figure 1. Out-of-bag AUC values for the predictions of different outcomes over 32 repeated validation folds.

In the models for pathological lymph node status and tumor stage, both EPE score and PI-RADS category had a large impact on the predictions, while none of the clinical variables appeared in the top eight for prediction of surgical marginal status or pathology-based ISUP grade group. In terms of important radiomic features, we had Laplacian of Gaussian ("log") features for surgical marginal status, local binary pattern ("lbp") features for pathological tumor stage, and wavelet features for ISUP grade group.

Conclusions: Our results illustrate that radiomics can have a significant impact on the prediction of the pathological features of prostate cancer. Validation on the larger cohort will reinforce these findings.

CO57

IMPACT OF INTER-OBSERVER VARIABILITY ON FIRST AXILLARY LEVEL DOSIMETRY IN BREAST CANCER RADIOTHERAPY - AN AIRO MULTI-INSTITUTIONAL STUDY

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Aims: To quantify the incidental dose received by the first axillary level (L1) in breast cancer locoregional treatment, including axillary levels (Ls) 2, 3 and 4.

Methods: Eighteen radiotherapy (RT) centres were asked to elaborate a locoregional treatment plan on their own planning target volume (PTV), namely Single Centre PTV (SC-PTV), created from the clinical target volumes (CTV) delineated in a previous investigation, i.e. Single Center CTV (SC-CTV). The SC-CTV comprised the axillary nodes of three patients with different anatomy (P1 with clear anatomy, P2 with obesity, and P3 with impaired arm mobility). Gold standard CTV (GS-CTV), comprising L2, L3 and L4, was generated from an expert consensus and validated with STAPLE algorithm; a gold standard contour for L1 was created with the same procedure. Each centre planned the treatment on their own SC-PTV, then replaced by the GS-PTV (GS-CTV expanded with margins applied by the single centre). All plans were imported into MIM software version 6.1.7 and dose-volume histograms (DVHs) were extracted. Kruskal-Wallis test was used to compare the populations.

Results: All plans but ones were performed with IMRT techniques. Among the available dosimetric parameters, near-min dose (D98), near-max dose (D2), and mean dose (Dmean) were chosen to analyze the *Results:* For P1, P2 and P3, respectively, median D98 was 47% (standard deviation, SD 16%), 49% (SD 17%), and 59% (SD 18%), median D2 was 100% (SD 4%), 100% (SD 5%) and 104% (SD 4%) and median Dmean was 77% (SD 8%), 75% (SD 10%) and 94% (SD 7%) (Figure 1). Overall, variations of the dose received by L1 were more pronounced for near-min dose with a SD ranging from 16 to 19% across all centers. As expected, L1 in patient with impaired arm mobility (P3) received statistically significant higher doses considering D2 ($p = .00163$) and Dmean ($p = .00019$) when compared to P1 and P2.

Conclusions: Overall, dose to L1 was higher in P3 than in P1 and P2, probably due to the different arm positioning, which moved such axillary level closer to the radiation treatment field on breast/chest wall and L2-L4. The results highlighted that L1 coverage by incidental dose was not negligible, even in case of highly conformal techniques. The potential consequences on the increased risk of toxicity and the contribution to local control on the nodal regions, especially in case of positive sentinel node and no dissection, need to be further investigated.

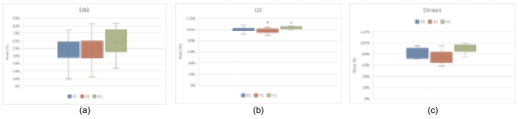

Figure 1. L1 coverage in terms of near-min dose, D98 (a), near-max dose, D2 (b) and mean dose, Dmean (c).

CO58

RE-IRRADIATION FOR IPSILATERAL BREAST TUMOR RECURRENCE IN ITALY: SURVEY BY THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims: The Re-irradiation and the Breast Cancer

Working Groups on behalf of the Italian Association of Radiation Oncology (AIRO) proposed a survey to provide an overview of the current management of breast cancer re-irradiation among Italian radiation oncologists.

Methods: On 25 October 2021 all the Italian radiotherapy centers surveyed by AIRO (n=183) received an online questionnaire focused on radiation oncologists' policies toward re-RT, during the previous two years (2019-2020), in three different scenarios: IBTR managed with second conservative surgery (9 questions); IBTR treated with mastectomy (7 questions); inoperable IBRT (5 questions). Surveyed radiation oncologist were also asked to answer to an initial part about general aspects (13 questions) and finally an expression of interest of being involved in a prospective observational trial of re-RT for BC was requested (1 question). The main topics investigated were: patient selection criteria, radiation techniques, volume and dose prescription, dose volume constraints, and drugs combinations.

Results: A total of 77 Italian radiotherapy centers answered the Survey (42.0% of all surveyed Italian centers): 47 from non academic hospitals, 12 academic hospitals, 15 IRCCS, 7 Nursing homes, 1 ARNAS. Sixty-four/77 centers declared to have performed "curative" re-RT for IBRT; 43/77 respondents administered re-RT after second BCS (mean 8.4, range 1-50 patients per center), 28/77 after mastectomy (mean 2.7, range 1-7 patients per center), and 25/77 for inoperable (mean 2, range 1-5 patients per center). Re-RT practice varied widely among centers as it concerns treatment volumes, dose and fractionation schedules, technique, and dose-volume constraints for organs at risks. For each scenario, the majority of respondents used external beam radiotherapy (EBRT) including 3DCRT, VMAT, IMRT, Tomotherapy. Forty-six/77 participants (59.7%) expressed their interest in participating to a prospective observational study of re-RT for breast cancer.

Conclusions: The survey demonstrated a widespread of interest in the possibility of re-irradiation for ipsilateral breast cancer recurrence. Nevertheless, practice of re-RT varied widely among centers highlighting the lack of guidelines and the need for further studies to define the best indications, techniques and fractionations.

CO59

PLAN QUALITY COMPARISON AT FIVE YEARS IN TWO COHORTS OF BREAST CANCER PATIENTS TREATED WITH HELICAL TOMOTHERAPY

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Aims: The aim of this analysis was to evaluate the quality of planned dose distribution in two groups of breast cancer patients treated at the same Institution with hypofractionated intensity-modulated radiotherapy (IMRT) delivered using Helical TomoTherapy®.

Table 1. Recap of the plans' scores (a) and summary of the planning objective constraints (b).

a)

	total score (points)	n plans 2012-2015 (%) N = 120	n plans 2019-2020 (%) N = 120	Δ
Optimal	6	85 (70.8)	95 (79.2)	+ 9.2%
Acceptable	5.5	22 (18.4)	18 (15)	-3.4%
Compromised	≤ 5	13 (10.8)	7 (5.8)	-5.0%

b)

Planning objective/constraint	Median value (IQR)_2012-2015	Median value (IQR)_2019-2020	Plans satisfying planning objectives/constraints 2012-2015 (%)	Plans satisfying planning objectives/constraints 2019-2020 (%)
PTVs Chest wall				
V95% ≥ 90%	94.9 (92-97)	96.3 (92.6-98.0)	85.8	90
V90% ≥ 95%	99 (97-99.8)	99.4 (98.4-100.0)	92.5	95
Dmean ≥ 99%	99.8 (99.5-100)	99.6 (99.4-99.8)	90.8	92.5
D0.03 cm3 ≤ 110%	107.7 (106-108.9)	106.6 (105.8-107.1)	90.8	97.5
V107% ≤ 30%	0.04 (0-0.3)	0 (0-0.01)	100	100
PTV svc				
V95% ≥ 85%	93 (87.2-96.1)	97.8 (96.3-98.8)	81.7	100
V90% ≥ 90%	97.7 (95.0-99.2)	99.4 (98.6-100)	91.7	100
Dmean ≥ 95%	98.8 (96.9-99.9)	99.1 (98.6-99.7)	91.7	100
D0.03 cm3 ≤ 110%	107.0 (105.0-108.2)	107.0 (105.6-108.2)	90	95
V107% ≤ 30%	0 (0-0.2)	0 (0-0.15)	100	97.5
OARs				
Ipsilateral lung				
D15% ≤ 31 Gy	27.0 (25.7-28.5)	26.30 (25.0-27.6)	100	99.2
D20% ≤ 26.4 Gy	23.8 (22.9-25.0)	23.25 (22.0-24.4)	96.7	99.2
D35% ≤ 17.6 Gy	16.0 (15.0-17.0)	15.3 (14.3-16.5)	96.7	99.2
D50% ≤ 13 Gy	11.5 (10.2-12.0)	11.2 (9.8-12.0)	99.2	98.3
Contralateral lung				
D20% ≤ 13 Gy	6.7 (5.2-8.1)	6.1 (5.3-7.3)	100	100
D35% ≤ 10.6 Gy	4.7 (4.0-6.0)	4.7 (3.7-5.4)	100	100
D50% ≤ 9 Gy	3.1 (2.3-4.0)	3.4 (2.4-4.1)	100	98.3
Contralateral breast				
D15% ≤ 17.6 Gy	7.5 (6.0-9.1)	7.6 (6.3-8.6)	100	100
D20% ≤ 9 Gy	6.5 (5.6-7.7)	6.5 (5.7-7.3)	98.3	97.5
D35% ≤ 6 Gy	4.9 (4.0-5.2)	4.7 (4.0-5.1)	97.5	97.5
D50% ≤ 4.4 Gy	3.9 (3.3-4.0)	3.7 (3.4-4.1)	95	97.5
Heart*				
D15% ≤ 17.6 Gy	12.0 (11.0-13.0)		100	-
D20% ≤ 13 Gy	10.8 (10.0-11.9)		100	-
Heart**				
D15% ≤ 8 Gy	6.1 (5.6-7.0)	6.3 (5.6-7.0)	100	97.5
D20% ≤ 6 Gy	5.1 (4.5-5.9)	5.1 (4.6-5.7)	97.9	93.3
Dmean ≤ 5 Gy	4.2 (3.8-4.7)	4.5 (3.9-4.8)	94.9	94.2
Brachial plexus				
D0.03 cm3 ≤ 59.6 Gy	38.8 (38.0-39.3)	39.1 (38.9-39.4)	94.2	96.7
Spinal cord				
D0.03 cm3 ≤ 17 Gy	13.4 (3.0-15.0)	15.0 (13.7-15.9)	98.3	100
Stomach				
Dmax ≤ 9 Gy	4.4 (2.2-8.8)	5.7 (3.0-9.9)		70
Dmean ≤ 2.6 Gy	1.3 (1.0-2.6)	1.2 (0.7-2.0)		91.7
Liver				
V13Gy ≤ 17%	3.7 (0.5-7.5)	3.0 (0.1-6.8)	-	100
Dmean ≤ 4.4 Gy	3.2 (1.6-4.1)	3.0 (1.5-4.0)	-	88.3
Oesophagus§				
Dmax ≤ 10 (2015) 15 (2020) Gy	7.9 (6.9-9.0)	14.8 (14.0-15.7)	91.2#	60.8
Humeral head‡				
Dmax ≤ 30 Gy	25.0 (19.0-28.0)	26.7 (24.0-28.6)	97.3	94.2

*Heart dose relative to the first 22 patients treated between May 2012 and April 2013
**Heart dose constraints relative to the remaining patients
§ The oesophagus dose constraint was evaluated on 113 plans in the 2015 group
‡ Humeral head dose distribution was evaluated on 110 plans in the 2015 group

Methods: Two groups of patients (half treated between 2012 and 2015 and half treated between 2019 and 2020) with implant-based immediate breast reconstruction (IBR) who received post mastectomy RT to the chest wall (CW) and to the infra/supraclavicular nodal region (SVC) using a 15-fraction schedule (2.67 Gy/fraction). The RT treatment was delivered using the TomoTherapy Hi-Art System (Tomotherapy® System, Accuray Incorporated, Sunnyvale, CA) in helical mode. Dose distribution was evaluated according to dosimetric indices extracted from dose-volume histograms (DVHs) selected from those employed in the clinical routine. A quantitative scoring tool, adapted from the one used by

Motwani et al., was employed to retrospectively compare the quality of the planned dose distribution between the sub-cohorts of the two treatment groups in terms of both target coverage and sparing of organs at risk (OARs).

Results: A total of 240 patients were included in the analysis. The distribution of total scores resulting from the summation of points and the distribution of planning objectives for planning target volume (PTV) coverage and for OAR sparing are reported in Table 1a. In particular, the percentage of optimal plans increased from 70.8% (2012-2015) to 79.2% (2019-2020), while the percentage of compromised plans decreased from 10.8% to 5.8%. Median values of dosimetric indexes, as well as the percentage of plans satisfying each planning objectives/constraint, both for the individual organs and target volumes, are reported in Table 1b.

Conclusions: In conclusion, our experience showed that Tomotherapy in helical modality provides a large proportion of optimal plans in terms of PTV coverage and OARs sparing, in a challenging population of postmastectomy patients with IBR. The learning curve showed that five years apart the rate of optimal plans was increased along with a decrease in the number of compromised plans. This analysis could be a useful platform to compare dose constraints between similar studies and to further refine them to optimize helical PMRT.

CO60

UPFRONT STEREOTACTIC RADIOTHERAPY WITH CYBERKNIFE FOR HER2+ BREAST CANCER PATIENTS: UPDATE OF MONOISTITUTIONAL EXPERIENCE WITH 82 METACHRONOUS BRAIN METASTASES

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Introduction: The aim of this study was to explore local control (LC), overall survival (OS), intra- and extracranial control in a mono institutional experience with stereotactic radiosurgery (SRS) for metachronous brain metastases of HER2+ breast cancer patients.

Materials and Method: Data of consecutive patients affected by brain metastases from HER2+ breast cancer who underwent SRS with CyberKnife (Accuray, USA) from February 2012 to November 2020 were retrospectively analysed. Parameters as demographics, histology and primary tumour characteristics, presence and control of extracranial disease, systemic treatment, modified breast GPA, number of lesions, single and total gross target volume (GTV) were collected. LC, OS, progression in brain (in field and out-field), extracranial progression disease and factors related were evaluated.

Results: Thirty-two patients with 82 lesions were included in the analysis. Median age at metastases treatment was 54 years (range 37-73). Median number of brain lesions was 2 (range 1-9). At the time of Cyberknife tretament, 9 patients had extracranial disease not in control, while all the patients received trastuzumab. Total median SRS dose was 21 Gy (range 15-24 Gy) given in 1 to 3 fractions, in alternate days. After a median follow-up of 19 months (range 12-44), at least one radiological evaluation was available for 30 patients (78 lesions). LC was reported in 69/78 treated lesions (88%) with 24-mo progression free from local failure (PFFLF) of 90% (range 76-96) (Figure 1). Median OS was 42 months (range 19-50) with 2-years OS of 66% (46-80). 20 patients had an out-field progression disease in brain with a 24-mo Proportion-free from Distant Intra-cranial Failure (PFFDIF) of 21% (7-40) while 20 patients had extracranial progression disease. Univariate analysis showed that the absence of controlled systemic disease at the time of SRS was associated with worse OS (p = 0.008). No difference between LuminalB/HER2+ and HER2 enriched biology was observed in term of LC, OS PD out field and extracranial control.

Conclusions: Our results showed an excellent LC for HER2+ brain metastases treated with SRS. In our experience, OS was in line with reported literature. The control of systemic disease at time of SRS was a prognostic factor in OS.

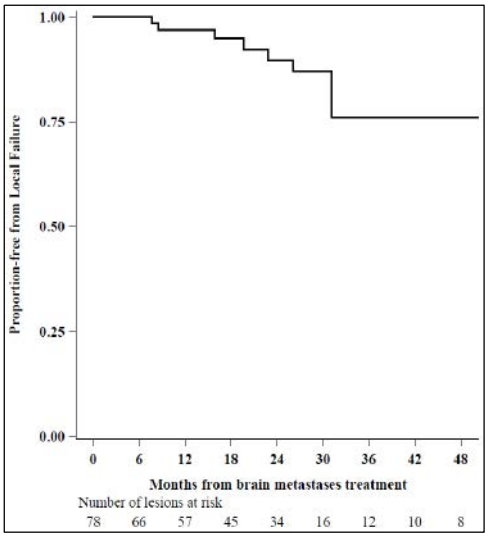

Figure 1. Kaplan-Meier estimate of progression free from local failure. Proportion-free from Local Failure (N=78 1) [1]. For 2 patients (4 lesions) there were no info about PD in-field: they were not included in this analysis.

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DEEP INSPIRATION BREATH HOLD (DIBH) IN PHOTON VOLUMETRIC MODULATED ARC THERAPY (VMAT) VERSUS INTENSITY MODULATED PROTON THERAPY (IMPT) FOR LEFT SIDED BREAST CANCER: A PRELIMINAR DOSIMETRIC ANALYSIS OF A HYPOFRACTIONATED REGIMEN (HYPO-RT)

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Aims: To compare exposure of organs at risk (OARs) and target dose distribution between photon Volumetric Modulated Arc Therapy (VMAT) and pencil-beam scanning Intensity Modulated Proton Therapy (IMPT) for left-sided breast cancer (LSBC) patients (pts) employing Deep Inspiration Breath Hold (DIBH) in the hypofractionated regimen (Hypo-RT).

Method: A dosimetric analysis on VMAT versus IMPT plans was performed. IMPT plans were generated on the initial CT scans. Dose to heart (mean heart dose -MHD), Left Anterior Descending Coronary Artery (D1 to LADCA -D1LADCA), lungs (V20 to homolateral lung -V20L- and mean dose to contralateral lung -MCL), contralateral breast (mean dose -MCB), if present, and oesophagus (mean dose -MOe) were retrieved. Target coverage was evaluated with the volume receiving 95% of the prescription dose (V95). Robust optimization was used for IMPT plan calculations on CTV with 5 mm isotropic setup error and a 3-5% range uncertainty. VMAT plans were optimized on PTV (CTV + 5 mm isometric expansion).

Results: Ten CT scans of LSBC pts were performed from March 2022 to June 2022. Target volumes consisted of whole breast in 3/10 pts and chest wall (with or without reconstruction with expander or prosthesis) in 7/10 pts. Regional lymph nodes were also contoured in 7/10 pts (6/10 sovra-infraclavear nodes and 1/10 internal mammary chain). Prescribed dose range was 40.05-42.4 Gy/15-16 fractions with a tumor bed boost (16 Gy/8 fractions) in 1 patient. Median target V95% was 99.35 (92.4-100) for VMAT versus 99.81 (97.13-100) for IMPT. OARs' doses comparisons between VMAT and IMPT were the following: median D1LADCA was 11.78 (5.48-18.16) vs 3.98 (0.24-15.46); median MHD was 3.24 (1.99-4.49) vs 0.12 (0.01-1.00); median V20L was 12.95 (5.72-16.45) vs 3.40 (0.73-15.72); median MCL was 2.93 (1.78-4.72) vs 0.15 (0.00-0.45); median MCB was 2.76 (1.39-2.89) vs 0.08 (0.00-0.18) and median MOe was 7.31 (1.61-13.29) vs 3.38 (0.00-4.49). Example of differences in dose distribution in Figure 1. IMPT significantly reduced OARs' doses (p-value < 0.001 at Student's t-test).

Conclusions: In clinical practice, Hypo-RT with VMAT DIBH for LSBC pts is a satisfactory option to spare OARs while ensuring optimal target coverage. In this preliminary analysis, we observed that IMPT significantly reduced the dose to OARs guaranteeing the target coverage. To establish a correlation with clinical outcomes a validation on a larger prospective cohort is warranted.

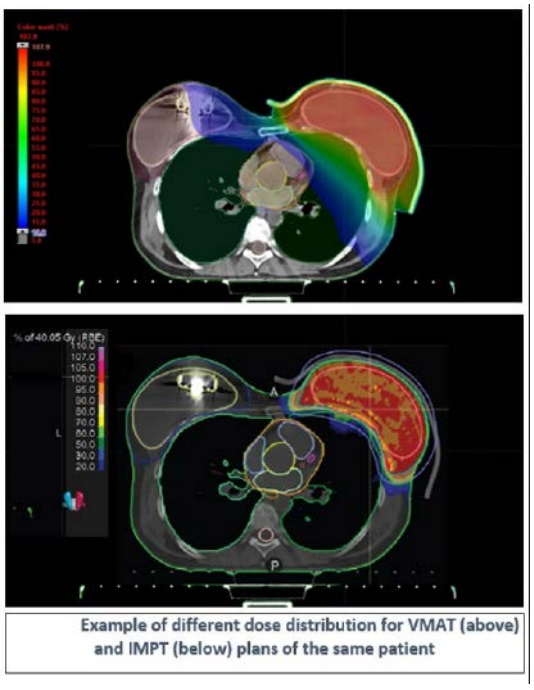

Figure 1.

CO62

SAFETY OF CYCLIN-DEPENDENT KINASE4/6 INHIBITOR COMBINED WITH RADIOTHERAPY HORMONE RECEPTOR POSITIVE BREAST CANCER

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Aims: Cyclin-dependent kinase (CDK)4/6 inhibitors are utilized in locally advanced or as first-line therapy for metastatic hormone receptor positive breast cancer. However, there are limited data on safety of combined radiotherapy (RT) and CDK4/ 6 inhibition.

Methods: We conducted a multicentric retrospective study of women with breast cancer who received palliative RT or adiuvant RT within 15 days of CDK4/6 inhibitor use. The primary endpoint was toxicity per Common Terminology Criteria for Adverse Events v5.

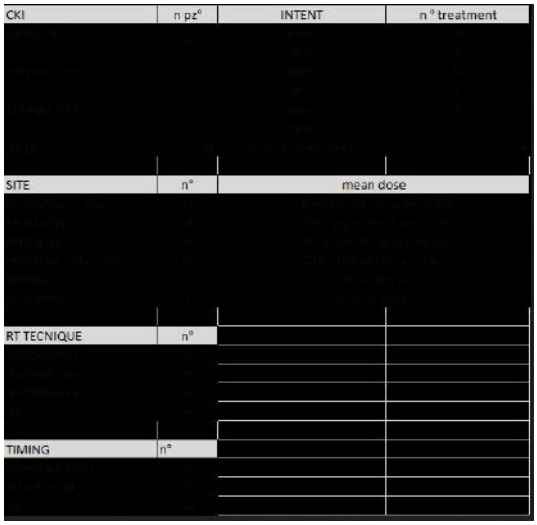

Figure 1.

Results: Fourty-one patients received therapy with CDK inhibitor: 22 with ribocilcib (54%), 17 with palbociclib (41%) and 2 with abemaciclib (5%). These patients underwent 50 courses of radiotherapy. Among RT treatment (50) 11 patients (22%) received radiotherapy on breast/chestwall with an adjuvant intent with a median dose of 50 Gy in 25 fractions. The Median RT dose for the metastatic site was 30Gy. Treated sites included brain (n=10, 20%), spine (n=14, 28%), other bony sites (n=13, 26%) and others (n=2, 4%). Metastatic sites were treated with 3D technique in 21 cases and with SRS/SRT in the other 18 cases. RT was delivered concurrently or sequential CDK4/6 inhibitors in 28 (56%) and 22 (44%) cases respectively. One acute grade 3 hematologic toxicity occurred with interruption of CDKi before the RT course. No increased hematologic toxicity was attributable to RT with no grade 3 hematologic toxicities rates before, during, and 2 weeks after RT completion.

Conclusions: The use of RT within 2 weeks of CDK4/6 inhibitors had low acceptable toxicity and high efficacy, suggesting that it is safe for palliation of metastatic breast cancer.

CO63

HEART AND LUNG COMPLICATION PROBABILITY IN PATIENTS WITH LEFT BREAST CANCER UNDERGOING CONSERVING SURGERY AND RADIATION THERAPY: COMPARISON BETWEEN FREE BREATHING AND DEEP INSPIRATION BREATH HOLD RT TECHNIQUE

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Aims: Postoperative radiation therapy (RT) for left-sided breast cancer patients may be cause of heart toxicity. Deep inspiration breath hold (DIBH) technique reduces cardiac radiation exposure. The aim of this study is to compare normal tissue complication probability (NTCP) between DIBH and free breathing (FB) techniques, analyzing dose distribution in heart and coronary arteries, and lung.

Method: Cardiac chambers and coronary arteries were delineated according to ESTRO guidelines on the simulation CT scans of 46 left-sided breast cancer patients having undergone conserving surgery and breast RT. The plans were simulated in both, FB and DIBH CT scan in each patient to be equivalent for target coverage, namely 95% prescription dose (40 Gy in 15 fractions on whole breast plus 10 Gy in four fractions on tumor bed when appropriate) to 95% of target volume. Dosimetric parameters for the heart, cardiac substructures and left-lung were retrieved and compared between DIBH and FB simulation plans. Four Lyman Kutcher Burman (LKB) models and one logistic model were applied to evaluate cardiac perfusion defects (Das et al., 2005), long-term cardiac mortality (Gagliardi *et al.*, 1996), pericardial effusions (Martel *et al.*, 1998), radiation-induced pneumonitis (Rancati *et al.*, 2007), and coronary stenosis (Moignier *et al.*., 2015) in both techniques. The relative risk (RR) was

evaluated as RR = (NTCP DIBH/NTCP FB).

Results: Whole heart and coronary arteries doses were significantly reduced in DIBH plans considering all dosimetric parameters. In particular, the heart mean dose (Dmean) and the heart maximum dose (Dmax) were reduced in DIBH approach by 37% and 58% respectively. All cardiac chambers reported a significative dose reduction of Dmean and near-maximum D2. The NTCP application showed a RR<1 considering perfusion defects (p=0.002), coronary stenosis (p=0.03), and pericardial effusions (p=0.000) and a significative reduction of radiation-induced pneumonitis in DIBH plans (p=0.005). Only for long-term cardiac mortality was not found a significative reduction in DIBH plans (p=0.301).

Conclusions: The dosimetric benefit of DIBH over FB therapy was consistently observed for all cardiac substructures. The DIBH technique promises a significant advantage in ameliorating the heart toxicity profile of left breast Irradiation.

CO64

ULTRA-HYPOFRACTIONED ADJUVANT RADIOTHERAPY IN PATIENTS UNDERGOING CONSERVATIVE SURGERY FOR EARLY BREAST CANCER

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Aims: A multicenter, retrospective and prospective observational study was designed to collect data of patients (pts) treated with an ultra-hypofractionated schedule of adjuvant whole breast radiotherapy (RT) in order to confirm the results of the FAST-forward trial1 in the clinical practice.

Methods: Primary endpoint: treatment safety in terms of acute and chronic toxicity. Secondary endpoints: survival outcomes and relapse rate, cosmetic result, quality of life (QoL). Inclusion criteria: early breast cancer, age ≥ 18 years, breast conserving surgery. Exclusion criteria: regional nodal RT, distant metastasis, history of previous malignancy. Pts receive 26 Gy in 5 consecutive fractions (fr); a sequential or a simultaneous integrated boost is delivered to the tumor bed (7.6 Gy in 2 fr or 30 Gy in 5 fr), according to clinical and pathological risk factors. Dose constrains are the same as in the FAST-forward study. Toxicity is evaluated using the Common Terminology Criteria for Adverse Events version 5.0, cosmetic results by photographs2 and Harvard Breast Cosmesis Grading Scale, QoL by EORTC QLQ-C3 and –BR23 questionnaires. The uni- and bi-varied statistical analysis was performed using the IBM-SPSS program version 16.

Results: From March 2020 to May 2022, 255 pts were enrolled from 3 Italian centers (Table 1). Median follow up was 7 months (range 1-25). Acute toxicity was recorded in 183/255 (71.8%) pts; cutaneous effects were observed in 165 pts and other events in 47 (some pts developed more than 1 toxicity). Most of the registered events were mild, just 25 pts developed G2 toxicity and only 1 G3 event was observed (Table 2). Late toxicity was recorded in 39.6% (57/144), 28.6% (22/77) and 16.7% (5/30) of pts at 6, 12 and 18 months respectively (Table 3). Toxicity was correlated with pts' age, tumor's characteristics (TNM, grading, bio-pathological profile), systemic therapy and dosimetric data. Acute toxicity was significantly associated with young age (p=0.000), while 6 months toxicity (p=0.032) with chemotherapy.

Conclusions: Having recorded predominantly G1 toxicity, our experience showed that the FAST-forward schedule is safe in terms of acute toxicity, but longer follow up is needed to confirm late toxicity results. We also expect to have more data as other 32 centers will participate in the study. Our favourable results lead us to adopt the 5-fractions scheme in our clinical practice, thus reducing pts access to the hospitals and the waiting lists.

Tables 1 - 2 - 3.

Table 1 – Patients characteristics	
Median age: 63 years (range 19-90)	
Histology	
in situ	39
invasive	216
T	
pTis	44
pT1	188
pT2	23
N	
pN0	204
pN1	29
pNx	22
Grading	
G1	69
G2	124
G3	53
Molecular subtype	
Luminal A	147
Luminal B	55
HER2 + (not luminal)	8
Triple negative	16
Systemic therapy	
Neoadjuvant CT	6
Adjuvant CT	47
Hormone therapy	194
Trastuzumab	19
None	38
Dose	
26 Gy	247
27 Gy	8
Boost	
Sequential	76
Simultaneous	0
None	179

Table 2 – Acute toxicity	
Erythema	
G1	80/255 (31.4%)
G2	8/255 (3.1%)
Skin ulceration	
G1	15/255 (5.9%)
G2	3/255 (1.2%)
G3	1/255 (0.4%)
Skin dyschromia	
G1	84/255 (32.9%)
G2	11/255 (4.3%)
Oedema	
G1	39/255 (15.3%)
G2	5/255 (2.0%)

Table 3 – Chronic/Late toxicity	
Erythema	
6 months	7/144 (4.9%)
12 months	4/77 (5.2%)
18 months	0/30 (0%)
Breast induration	
6 months	17/144 (11.8%)
12 months	6/77 (7.8%)
18 months	1/30 (3.3%)
Skin dyschromia	
6 months	27/144 (18.8%)
12 months	7/77 (9.1%)
18 months	0/30 (0%)
Oedema	
6 months	22/144 (15.3%)
12 months	9/77 (11.7%)
18 months	5/30 (16.7%)

CO65

WHICH ROLE FOR 11C-METHIONINE PET IN RADIOTHERAPY PLANNING IN NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS?

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Aims: We investigated the role of [11C]-methionine PET (11CMETPET) in a cohort of newly diagnosed glioblastoma multiforme (GBM) patients to evaluate whether it could improve radiotherapy (RT) volume delineation.

Methods: Newly diagnosed GBM patients, ages 18–70, with a Karnofsky performance scale(KPS) ≥70 with available MRI and 11CMETPET were included. Patients were treated with surgery followed by radio-chemotherapy. For RT planning CT scan, T1-weighted FLAIR (fluid-attenuated inversion recovery images) and T2-weighted 3D-FLAIR followed by T1-weighted MPRAGE MRI and 11CMETPET were acquired within 1 month from surgery. These images were co-registered using iplannet system (Brainlab AG, Munich, Germany). Two different clinical target volume (CTV) were outlined: CTV1 corresponded to the entire surgical cavity plus the residual tumor after surgery or the abnormality on the T1-weighted post-contrast MPRAGE and MET PET in the case of biopsy; in cases of uptake on 11CMETPET outside of the surgical cavity or residual tumor, it was included in CTV1. CTV2 corresponded to the abnormality on FLAIR MRI images after surgery and included, in all cases, CTV1 and 11CMETPET uptake. Planning target volumes 1 and 2 (PTV1/PTV2) were generated, adding an isotropic margin of 5 mm from CTV1 and CTV2, respectively. The dose prescribed was 60 Gy on PTV1, and 42 Gy on PTV2 for 15 days, using a simultaneous integrated boost. The role of 11CMETPET in RT planning was analyzed. A threshold of SUVmax was searched.

Results: From August 2013 to April 2016, 93 patients were treated and included in this analysis. Residual tumor volume was detected in 63 cases on MRI and in 78 on 11CMETPET, including 15 receiving gross total resection. The 11CMETPET uptake was mainly located in FLAIR abnormalities. Concerning RT, in all cases, the whole biological target volume (BTV) was inside the CTV1, while in 10 (11%) patients, part of the BTV was outside the CTV1 in the FLAIR abnormalities area, and the CTV1 was modified in relation to the 11CMETPET uptake. The presence of [11C]-methionine uptake in patients receiving gross total resection proved to influence survival (p=0.029). The threshold of the SUVmax conditioning outcome was five.

Conclusions: 11CMETPET allowed to detect areas at higher risk of recurrence located in FLAIR abnormalities in patients affected by GBM. A challenging issue is represented by integrating morphological and functional imaging to better define the target volume.

CO66

STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES FROM RENAL CELL CARCINOMA: OUTCOME EVALUATION AND PROGNOSTIC FACTORS ASSESSMENT. A MULTICENTER RETROSPECTIVE STUDY

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Aims: In patients with brain metastases from renal cell carcinoma (BM-RCC), the prognosis is poor and their management is a challenge. When the number and/or the volume of metastases are limited, local treatment is required: radiosurgery (SRS), hypofractionated radiosurgery (HSRS) exclusive or after surgery. We evaluated the clinical outcomes of a large series of BM-RCC patients treated in three Italian centers using stereotactic radiotherapy (SRT).

Methods: We analyzed patients with brain metastases (BMs) from kidney cancer treated with SRS or HSRS on up to 4 lesions. CT scan and enhanced T1MRI sequences were acquired and coregistered for radiation therapy planning. Different total doses and fractionation were delivered: 24-25Gy/1fraction, 20Gy/1fraction, 21Gy/3fractions, 32Gy/ 4fractions, 30Gy/5fractions based on metastases volume and diameter, 27-30Gy/3fraction in cases of adjuvant HSRS after surgery. Efficacy was evaluated in terms of local control (LC) and overall survival (OS). Prognostic factors related to OS were analyzed too.

Results: One hundred-forty BM-RCC patients for a total of 208 lesions treated were evaluated. Thirty-five (25%) were female and 105 (75%) male with a median age of 64 years (range 37–90 years). The greater number of patients had a disease-specific-graded-prognostic-

assessment (DS-GPA) score 3.5-4 (53.6%). Ninty-two (65.7%) of patients had one brain lesion. The median follow-up time was 62 months (range 8-227 months). At time of SRT, 121 (86.4%) patients had extracranial metastases. Surgery plus SRS have been performed in 17(8.2%) cases, SRS in 160 (76.9%), and HSRS in 31 (14.9%). Eighty-one (57.8%) patients received systemic therapy after stereotactic radiotherapy. Median LC was not reached, while local control at 6 and 12 months were 98.5% and 93.0%, respectively. No severe neurological toxicity occurred. Median OS was 15 months, 6 and 12 months overall survival rate were 73.3% and 53.2%, respectively. Age, number of BMs, DS-GPA score, combined local treatment (surgery plus adjuvant HSRS) and administration of systemic therapy after SRT, were observed as conditioning survival.

Conclusions: SRT have proven to be an effective local treatment for BM-RCC. Multidisciplinary evaluation and careful assessment of prognostic factors are useful for the optimal therapeutic choice.

CO67

PETTERN OF PRACTICE IN LATE ELDERLY PATIENTS WITH HPV POSITIVE OROPHARYNGEAL CANCER: A MULTICENTER RETROSPECTIVE STUDY ON BEHALF OF THE HEAD AND NECK CANCER STUDY GROUP OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL CLINICAL ONCOLOGY (AIRO)

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Aims: In contrast to the prevalent population of young patients (pts) in good general conditions with Human Papilloma Virus (HPV) positive oropharyngeal cancer (OPC), recent epidemiologic trends highlighted a rise of the disease incidence in the elderly population. Pts with ≥75 years of age are considered as "late elderly. The purpose of our work was to assess the pattern of practice across Italian centers in this patient group.

Table 1.

Population General Characteristic

Characteristic	
Sex	
male	52
female	18
ECOG PS	
0	26
1	32
2	12
Smokers	
never	22
<10p/y	13
10-20p/y	12
>20p/y	23
Not Stated	13
Stage	
I	20
II	19
III	31
Age	
Median (range)	78.68 years (75-86)

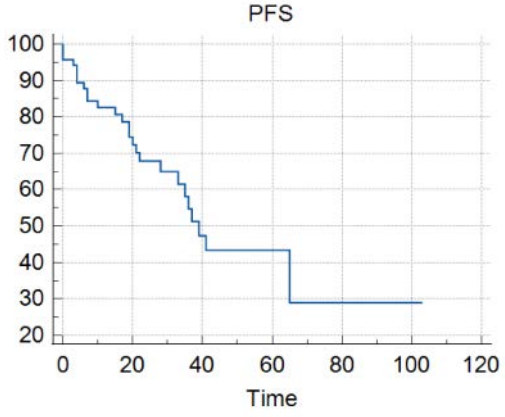

Figure 1.

Methods: This is an observational, non-interventional, multicenter, retrospective study. Pts were included if had a histologically-confirmed diagnosis of squamous cell OPC, age > 75 years at time of initial diagnosis, clinical stage of disease I-III (according to TNM/AJCC 8th edition), positive HPV status (p16 immunohistochemistry/HPV DNA-in situ hybridization) and if received

curatively-intended treatment, consisting of either intensity modulated radiotherapy (IMRT) alone (total dose > 50 Gy BED), concomitant chemo-radiotherapy (RTCT), induction chemotherapy (CT) followed by IMRT alone, or brachytherapy for early stage disease. Acute toxicity was evaluated according to CTCAE v5.0. Survival outcomes were estimated by the Kaplan-Meyer method.

Results: Seventy pts were included in this preliminary analysis. At time of diagnosis, the median age was 78 years (range 75-86). In 44% of the cases, pts received definitive IMRT. Concomitant RTCT, brachytherapy and induction CT followed by IMRT were administered to 27%, 18% and 11% of pts, respectively. In regards to acute toxicity, an overall 50% rate of >G3 events was observed, namely mucositis, radiation dermatitis and dysphagia in 26%, 13% and 11% of patients, respectively. At a median follow-up of 18.5 months (IQR 0-65), the median progression free survival and overall survival were 18 and 19 months, respectively. Disease progression was reported in 23 pts (33%), consisting of distant metastases (30%), nodal recurrence (26%), second primary cancer (13%), local recurrence (8%) and both locoregional and distant metastases (17%). Locoregional control was achieved in 62% of pts. Four pts (6%) died due to complications of treatment-related toxicities and 15 pts (21%) due to disease progression.

Conclusions: Our retrospective study confirms that definitive IMRT or RTCT are employed in late elderly pts with HPV- positive OPC, as in their younger counterparts, with similar rates of acute toxicity and oncological outcomes. Prospective studies in larger cohorts of geriatric pts are warranted in order to confirm our findings.

CO68

SUPERO: SUPPORTIVE CARE IN RADIATION ONCOLOGY FOR MULTIDIMENSIONAL MANAGEMENTE OF ONCOLOGICAL FRAILTY

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Aims: In radiotherapy as in the field of oncology in general, we are seeing an increase in patient complexity. With the aging of the population, there is an incremental growth in the incidence of elderly patients with cancer. The complexity of elderly patients, characterized by comorbidities, polypharmacy and disability, is combined with the sophistication of new treatments, making the cancer patient's pathway insidious.

Methods: In our Center, we have developed a continuum of care for complex patients by combining the Department of Geriatrics public facilities and the Radiation Oncology Center. Supportive care and geriatric oncology pathway were developed to manage patients at all stages of treatment, aimed at improving compliance by reducing treatment toxicity. The program provides ad hoc outpatient clinics, an inpatient ward, and timely management of patients who have accessed the emergency room. Patients are evaluated before each treatment, followed up, and taken care in case of toxicity through serial outpatient follow-ups and inpatient admissions, managed by the same team. The multidisciplinary team consist of four radiation oncologists, a dermatologist, an endocrinologist, two psychologists, two rehabilitation physician, anesthesiologists for pain therapy and nurses, coordinated by two geriatricians.

Results: In 2021, 1196 patients have been assessed. 847 were admitted for toxicity or to undergo oncological treatments. 349 patients were evaluated within the outpatient clinic of geriatric oncology and supportive care, for a total of 597 visits (258 first contact and 339 follow-up); within the geriatric oncology clinic mean age was 75 years; all patients aged ≥ 65 years old were assessed by a comprehensive geriatric assessment: 59.2% were fit, 31.6% vulnerable, and 9.2% frail. The reasons for outpatient assessment are shown in Figure 1. Cancer type is shown in Figure 2. For all radiotherapy patients and to complete the supportive care service, there are a rich range of outpatient services whose specifications and flows are shown in Table 1.

Conclusions: In conclusion, we think that an integrated service of supportive care is essential for the modern cancer patient who is often a complex patient for age or medical issues and needs multidisciplinary and multidimensional management in order to avoid over and under treatment, improve treatment compliance, and ensure the best treatments with the best quality of life.

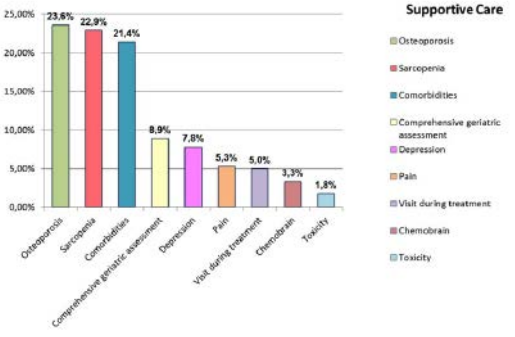

Figure 1.

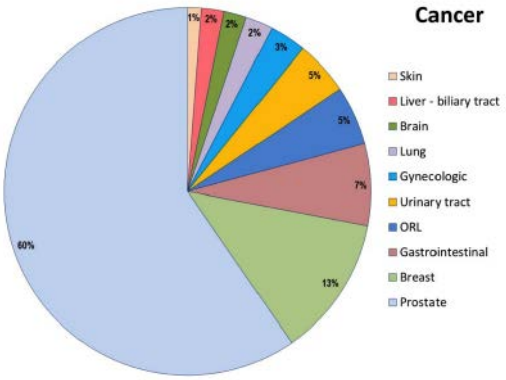

Figure 2.

Table 1. Outpatient services.

		Number of visits in 2021
Geriatric oncology	Comprehensive Geriatric Assessment Management of comorbidities in frail patients Management of osteoporosis and sarcopenia	597
Supportive care	Management of toxicities during treatments (fatigue, nausea, vomiting, dyspepsia, constipation, diarrhea, fecal and urinary incontinence, dysphagia, xerostomia, neurological disorders)	
Tegument toxicity and Functional aesthetics in oncology Advanced wound medication	Multidisciplinary management of skin and mucosal toxicities during radiotherapy or chemotherapy Daily nursing dressing	231
Pain	Multidisciplinary management of cancer pain	257
Endocrine and sexual dysfunction	Specialist management of endocrinological and sexual dysfunction during radiotherapy or hormone therapy	315
Psycho oncology	Psychological support during treatment	170
Rehabilitation	Evaluation and prescription of rehabilitation before, during, and after cancer treatments	Opened from February 2022

CO69

IMPACT OF GERIATRIC ASSESSMENT ON QOL OF ELDERLY ONCO-HEMATOLOGIC PATIENTS (ONCO-AGING) CANDIDATE TO COMPLEX TREATMENTS

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Aims: The ONCO-AGING study aims to test the impact of the Comprehensive Geriatric Assessment (CGA) on the quality of life (QoL) of elderly onco-haematological pts candidates for multimodality therapies, that resulted fragile at the G8 screening. Moreover, this study aims to assess some biological factors that can interfere with cancer immunity and cellular senescence. We investigate the impact of T cells senescence and myeloid-derived suppressor cells (MDSC) in the peripheral blood of enrolled patients on cancer progression and outcome.

Methods: Pts aged > 65 years candidate to first line therapy with biological target drugs or integrated radiotherapy will be screened for frailty by the G8 test. Those patients classified as frail (G8 < 14/17) are randomized to undergo CGA or standard of care (no CGA), prior to the start of therapy. The primary endpoint is QoL, assessed by EORTC QLQ-C30C. We also evaluate the potential prognostic/predictive role of MDSCs and cell senescence in the peripheral blood on 2 time-points: at baseline and at disease progression.

Results: From December 2019 to February 2022 we enrolled 155 pts. The median age is 75 years (range 65-91). The 61,9% (96/155) are male. The 46,5 % of pts (72/155) have more than 4 comorbidites and the 70,9% (110/155) chronically take more than 4 drugs other than those related to oncological therapies. The median G8 score is 12/17 (range 3-14). The 52.2% (81/155) has solid tumors (lung cancer 14,2%; breast cancer 6,45%, colorectal cancer 7,1%; melanoma 9,68%; genito-urinary cancer 4,52%, head and neck cancer 2,58%) and 47,8% (74/155) are affected by oncohematological diseases (myeloma 10,3 %, aggressive lymphoma 10,9 %, indolent lymphoma 4,52%, acute leukemia 8,38%, others 13,7%). The 23,9% of patients were treated with radiotherapy. The median baseline score of QoL was 66,6 points. To date, 24/155 patients enrolled are dead. The analysis of the impact of CGA on elderly onco-hematologic patients' outcome and QoL and the evaluation of MDSCs on liquid biopsies to assess the potential prognostic value of imbalance of immune-competent cells are still ongoing.

Conclusions: This trial will contribute to define the impact of CGA on the management of elderly onco-hematologic patients' candidate to complex therapies.

CO70

CORRELATION BETWEEN CHARLSON COMORBIDITY INDEX AND ACUTE TOXICITY IN ELDERLY PATIENTS (AGED ≥75) TREATED WITH CURATIVE INTENT RADIOTHERAPY, MANAGED BY A MULTIDISCIPLINARY ONCOGERIATRIC MODEL

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Aims: Aging is considerably related to several comorbidities, but little is known about efficacy and toxicity of radiation therapy (RT) in the elderly patients since the latter are under-represented in clinical trials and data is limited to patients with fewer comorbidities. The detection of predictive factors of toxicity associated to a multidisciplinary management could allow a tailored treatment for these patients. In this study, we aimed to evaluate the correlation between acute toxicity and Charlson comorbidity index (CCI) in elderly (≥75years) treated with curative RT.

Methods: A prospective observational study was designed in our Center for all patients with≥75years, candidate for curative RT. These patients underwent Geriatric8 questionnaire (G8q), before and at the end of RT. Patients with G8 score ≤14 were evaluated by a multidimensional geriatric assessment, investigating cognitive, functional, and nutritional domains, to define the frailty phenotype. Acute toxicity was evaluated by RTOG scale up to three months of the end of treatment. An analysis of correlation between the baseline CCI score calculated for each patient and acute RT toxicity was performed. Statistical analysis was performed using Fisher exact test for continues variables and the nonparametric Kruskal–Wallis test for categorical variables. P-values lower than 0.05 were considered significant.

Results: G8q was administered to 130 patients. Forty-seven of them (36.7%) resulted frail with a baseline G8 score≤14 (range 4-14); 31 of them underwent a multidimensional assessment. Acute toxicity grade≥2 was observed in 45 patients (47%). We evaluated associations between CCI score, G8 score and acute toxicity (Table 1). Charlson comorbidity index resulted 5, 6 or 7 in 121 patients (93%) and≥8 only in 9 patients (7%). The G8 score performed before and after treatment did not change according to the baseline CCI score and no correlation was observed between CCI score and toxicity (p=0.43). Male sex resulted to have an impact on acute toxicity, maybe related to the higher percentage of prostate cancer patients, treated with RT, that present acute events (p=0.07).

Conclusions: Our analysis did not show a correlation between CCI score and acute toxicity in elderly patients≥75years. The multidimensional evaluation resulted useful to obtain compliance to the treatment without increased toxicity. The study is currently ongoing.

Table 1. Population stratified for acute toxicity.

	Overall	no	yes	p
n	130	34	96	
Age (median [IQR])	79 [77, 81]	79 [77, 82]	79 [77, 81]	0.86
Sex= male (%)	82 (63)	28 (82)	54 (56)	0.007
Surgery = yes (%)	53 (41)	15 (44)	38 (40)	0.69
Wbc (median [IQR])	7 [5, 8]	7 [5, 8]	6 [5, 7]	0.27
Lymph (median [IQR])	2 [1, 2]	2 [1, 2]	2 [1, 2]	0.63
Neut (median [IQR])	4 [3, 4]	4 [3, 5]	4 [3, 4]	0.80
Plt (median [IQR])	202 [176, 238]	204 [163, 242]	202 [179, 234]	0.68
Hb (median [IQR])	13 [12, 14]	13 [12, 15]	13 [12, 14]	0.79
BMI (median [IQR])	27 [24, 29]	25 [23, 28]	27 [24, 29]	0.07
G8 baseline (median [IQR])	15 [14, 16]	15 [14, 16]	15 [14, 16]	0.46
Frailty baseline (%)				0.60
Fit	12 (9)	4 (12)	8 (8)	
Frail	2 (2)	1 (3)	1 (1)	
Vulnerable	17 (13)	5 (15)	12 (12)	
Not frail	99 (76)	24 (71)	75 (78)	
G8.post-RT (median [IQR])	15 [14, 16]	15 [14, 16]	15 [14, 16]	0.42
G8.geriatric baseline (median [IQR])	13 [11, 14]	13 [11, 15]	13 [11, 14]	0.47
Comorbidity number (median [IQR])	2 [1, 3]	2 [1, 3]	2 [1, 2]	0.95
Comorbidity number (%)				0.80
0	10 (8)	4 (12)	6 (6)	
1	41 (32)	9 (26)	32 (33)	
2	45 (35)	11 (32)	34 (35)	
3	25 (19)	8 (24)	17 (18)	
4	8 (6)	2 (6)	6 (6)	
5	1 (1)	0 (0)	1 (1)	
Radiotherapy intent (%)				0.11
Adjuvant	47 (36)	9 (26)	38 (40)	
Neo-adjuvant	15 (12)	2 (6)	13 (14)	
Exclusive	68 (52)	23 (68)	45 (47)	
Total dose (median [IQR])	5500 [5000, 7000]	5000 [4001, 6600]	5500 [5000, 7000]	0.03
Chemotherapy baseline= yes (%)	88 (68)	22 (65)	66 (69)	0.67
CCI score (median [IQR])	6 [5, 6]	6 [5, 6]	6 [5, 6]	0.43

CO71

TOXICITY AND OUTCOMES IN ELDERLY ANAL CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY: A SUBGROUP ANALYSIS OF A MULTICENTER STUDY ON BEHALF OF AIRO GASTROINTESTINAL STUDY GROUP

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Aims: Concurrent chemo-radiotherapy (CRT) is the standard treatment for anal cancer. Intensity-modulated radiotherapy (IMRT) was proved to reduce severe acute and late toxicities. For elderly patients' treatment needs often to be modified. Alternative treatment strategies are not described in guidelines and little evidence is available in the literature. Based on these considerations, we have analysed toxicity and treatment outcomes in patients≥70 years with anal cancer treated with curative CRT.

Methods: In 2020 a multi-institutional retrospective study was conducted to evaluate the pattern of care and clinical outcomes of anal cancer patients treated with IMRT techniques. Subgroup analyses according to the distribution of variables in Age subgroups (<70 years, n=694 and ≥70 years, n= 283) was conducted. The univariate Cox proportional hazards model reports the hazard ratio (HR) and the 95% confidence interval (95% CI) for Age (<70 vs. ≥70), ECOG PS (≥1 vs. 0), HIV (Yes vs. No), HPV (Yes vs. No) and baseline Haemoglobin level (Hb <10 vs. ≥ 10) as independent factors impacts on clinical outcomes: Overall Survival (OS) and Disease-Free Survival (DFS).

Table 1.

Table 1: Distribution of variables and toxicity in Age subgroups. The association between categorical variables was assessed using the chi-square test, and the p-value was reported, indeed, the Mann U Whitney test was used to assess median differences.

	Age		
	<70	≥70	*p-value*
	N=694	*N=283*	
Gender			*0.139*
Male	206 (29.7%)	70 (24.7%)	
Female	488 (70.3%)	213 (75.3%)	
Baseline ECOG performance status			*<0.001*
0	582 (83.9%)	181 (64.0%)	
1-2	109 (15.7%)	100 (35.3%)	
HIV			*<0.001*
Yes	506 (72.9%)	237 (83.7%)	
No	88 (12.7%)	1 (0.35%)	
NR	100 (14.4%)	45 (15.9%)	
HPV			*0.069*
Yes	143 (20.6%)	66 (23.3%)	
No	175 (25.2%)	52 (18.4%)	
NR	376 (54.2%)	165 (58.3%)	
Baseline Haemoglobin level			*0.247*
<10 g/dl	20 (2.88%)	10 (3.53%)	
>10 g/dl	456 (65.7%)	170 (60.1%)	
NR	218 (31.4%)	103 (36.4%)	
Concomitant chemotherapy			*<0.001*
No	18 (2.59%)	34 (12.0%)	
Yes	676 (97.4%)	249 (88.0%)	
NR	218 (31.4%)	103 (36.4%)	
Treatment interruption >5 days			*0.929*
No	564 (81.3%)	230 (81.3%)	
Yes	130 (18.7%)	53 (18.7%)	
Median Overall treatment time	44.0 [38.0;50.8]	43.0 [38.0;49.0]	*0.111*
ACUTE >G3 TOXICITY			
Skin	191 (27.5%)	59 (20.8%)	*0.154*
Intestinal	46 (6.63%)	18 (6.36%)	*0.701*
Urogenital	3 (0.43%)	2 (0.71%)	*0.601*
Hematologic	65 (9.37%)	20 (7.07%)	*0.605*
LATE >G3 TOXICITY			
Skin	2 (0.29%)	0 (0.00%)	*0.151*
Subcutaneous tissue	2 (0.29%)	1 (0.35%)	*0.022*
Intestinal	11 (1.59%)	7 (2.47%)	*0.074*
Urogenital	4 (0.58%)	0 (0.00%)	*0.330*

Legend: ECOG=Eastern Cooperative Oncology Group; NR= not reported.

Results: Older patients were more likely to have worse baseline performance status (PS 1 or 2) (35.3% vs. 15.7%, p <0.001), and more HIV+ status (82.7% vs. 72.9%, p <0.001), but otherwise baseline characteristics were similar. Older patients received less concomitant chemotherapy (88.0% vs. 97.4%, p <0.001) with similar compliance in terms of overall treatment times and treatment interruptions. No statistically significant increase has been reported in grade ≥3 acute and late toxicities in older patients (Table1). Stratifying by age, the probability of surviving 60 months was 85.6% (SE=1.70%) for age <70 years and 75.7% (SE=3.41%) for age ≥70 years (p=0.0001); for DFS was 78.30% (SE=1.93%) for age <70 years and 68.10% (SE=3.91%) for age ≥70 years (p= 0.0033). In patients with age ≥70 years a statistically significant association was found between HIV positive status and Hb <10 with OS and between Hb <10 and DFS.

Conclusions: In our analysis older patients who underwent CRT showed the same rates of grade ≥ 3 acute

and late toxicities compared to younger patients. OS and DFS resulted significant lower in patients with age ≥70 years. Baseline haemoglobin level <10 gm/dl resulted predictive of worse OS and DFS, suggesting that a supplement supportive therapy in elderly patients may be necessary.

CO72

EXTREME HYPOFRACTIONATED LINAC-BASED STEREOTACTIC RADIOTHERAPY FOR ELDERLY PROSTATE CANCER PATIENTS: PRELIMINARY RESULTS OF A PHASE II TRIAL

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Aims: Stereotactic body radiation therapy (SBRT) with extreme hypofractionation is replacing prostatectomy mostly in case of low-risk prostate cancer (PC). However, in selected case of intermediate/high risk, it could be a treatment justified solution. Aim of this study is to evaluate safety and efficacy of Linac-based SBRT in elderly patients affected by PC.

Method: Men aged 70 years or older affected by localized PC were enrolled and analyzed. The SBRT schedule consisted of 35 Gy in 5 fractions administered with Volumetric arc therapy in 1 or 2 weeks based on target volume and urinary symptom. According to risk group androgen deprivation therapy (ADT) was prescribed in some cases. Toxicity was assessed at the end of treatment, 2 weeks after SBRT and during follow-up (FU) using the Common Terminology Criteria for Adverse Events (CTCAE). PSA values were recorded before treatment and during FU as biochemical response criteria.

Results: Between July 2019-September 2021, 111 patients were treated. Median age was 77 years (range 70-86); 33% were in low-risk group, 48% in favorable/unfavorable intermediate-risk group and 19% in high-risk group. Median pre-treatment PSA was 6.61 ng/ml (range 0.2-40 ng/ml). ADT was administrated in 58 patients. Median PTV was 99.5 cc (range 51-192.2). Median baseline IPSS (International Prostatic Symptom Score) was 6 (range 0-19). At the end of treatment, no >G1 acute toxicity was observed. At 2-3 weeks after treatment, 3 patients reported G2 acute genitourinary toxicity (urinary frequency, urinary tract pain and urinary retention), while 14 patients referred rectal tenesmus. During the last FU, no late toxicity and no relevant deteriorations of QoL were described. At a median FU of 23 months (range 8-35), excellent biochemical disease control was achieved in all cases with median PSA of 0.5 ng/ml (range 0-6.46).

Conclusions: Linac-based SBRT in elderly patients affected by localized PC is feasible and well tolerated with excellent biochemical disease control.

CO73

ATX-101, A PEPTIDE TARGETING PCNA, HAS ANTITUMOR EFFICACY ALONE OR IN COMBINATION WITH RADIOTHERAPY IN MURINE MODELS OF HUMAN GLIOBLASTOMA

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Cell proliferation requires the orchestrated actions of a myriad of proteins regulating DNA replication, DNA repair and damage tolerance, and cell cycle. Proliferating cell nuclear antigen (PCNA) is a master regulator which interacts with multiple proteins functioning in these processes, and this makes PCNA an attractive target in anticancer therapies. Here, we show that a cell-penetrating peptide containing the AlkB homolog 2 PCNA-interacting motif (APIM), ATX-101, has antitumor activity in a panel of human glioblastoma multiforme (GBM) cell lines and patient-derived glioma-initiating cells (GICs). Their sensitivity to ATX-101 was not related to cellular levels of PCNA, or p53, PTEN, or MGMT status. However, ATX-101 reduced Akt/mTOR and DNA-PKcs signaling, and a correlation between high Akt activation and sensitivity for ATX-101 was found. ATX-101 increased the levels of γH2AX, DNA fragmentation, and apoptosis when combined with radiotherapy (RT). In line with the in vitro results, ATX-101 strongly reduced tumor growth in two subcutaneous xenografts and two orthotopic GBM models, both as a single agent and in combination with RT. The ability of ATX-101 to sensitize cells to RT is promising for further development of this compound for use in GBM.

CO74

NEUROTROPHIN-INDUCED EFFECTS ON MUCOSAL MELANOMA CELLS AFTER EXPOSURE TO LOW AND HIGH-LET RADIATIONS

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Aims: Mucosal melanomas originating from the gynaecological tract are a very rare and aggressive histology characterized by an intrinsic radio-chemoresistance. Cancer cells have an innate ability to actively migrate along nerves in a mechanism called perineural invasion, which is supported by neurotrophic factors such as neurotrophin-3 (NT-3), secreted in the tumour microenvironment. Although recent studies have demonstrated that C-ion radiotherapy (CIRT) could represent an alternative treatment option, only a few data regarding the effects of radiation on perineural invasion in relation to NT-3 are available in the literature. This study aims to investigate the response of malignant melanoma cells to NT-3, as well as to evaluate the effects of conventional X-rays radiotherapy (XRT) and CIRT on cell viability, proliferation and migration.

Method: Human vaginal mucosal melanoma (HMV-II) cells were irradiated with 2 Gy and 4 Gy of 6MV X-rays and C-ions. Cell viability was assessed with trypan blue exclusion method and proliferation was evaluated using the Olympus Provi TM CM20 incubation monitoring system. The migration ability was evaluated by means of scratch and Boyden chamber assays for control and irradiated cells, with and without the presence of NT-3. In the case of the transwell assay, NT-3 was added either in the lower compartments or in the upper ones to determine whether it induces migration or acts as a chemoattractant.

Results: After 4 Gy-XRT exposure the viability and the proliferation of HMV-II cell initially decreased, but eventually returned to those of non-irradiated cells after 3 days, while CIRT induced a significant decrease already measurable at the first time point of 24 hours and persisted for the whole-time interval observed. In particular, photon-irradiated cells reached confluence 5 days after the exposure, while 6 days after CIRT treatment the 4 Gy irradiated cells reached 87% of confluency. The addition of NT-3 leads earlier to confluence (i.e. 90% at 6 days). The migration of HMV-II cells decreased in a dose-dependent way for both the beams used (XRT vs CIRT) and NT-3 acted more as chemo-attractive effector (0 Gy $P<0.0003$, 2 Gy $P<0.0001$, 4 Gy $P<0.0001$) than as migration inducer.

Conclusions: We found that C-ions significantly reduce cell viability, proliferation and migration of mucosal melanoma cells in a dose-dependent way, while the presence of NT-3 can improve these biological abilities, even after radiation exposure. Understanding the mechanism of radioresistance and tumour escape of this rare tumour might pave the way to a tailored and more effective treatment.

CO75

INHOMOGENEOUS HIGH RADIATION DOSE DELIVERY BY LATTICE APPROACH TO HYPOXIC AND NORMOXIC AREAS IN BULKY TUMOURS: LATTICE_01, A MULTICENTRIC STUDY

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Aims: To evaluate feasibility, clinical response (CR), overall survival (OS) and toxicities in Stage IV patients with bulky tumour treated with LATTICE technique, delivering an inhomogeneous high radiation dose to different areas within the gross tumour volumes (GTV). This approach aimed to stimulate abscopal effect and to activate bystander effect on the nearby normoxic areas.

Patients and Methods: From June 2020 to May 2022 we selected all metastatic patients with bulky tumour both unresectable and unsuitable to ablative radiotherapy in the experimental centers. All patients showed Karnofsky Performance Status (KPS) ≥60, a life expectancy ≥6 months and permissive clinical/biochemical parameters.

Results: Forty-six patients (32 male and 14 female) with histological diagnosis of primary tumour and radiological evidence of systemic disease were enrolled. The median age was 76 years (range 26-91); before the treatment, all patients performed contrast-enhanced CT, 18F-PET/CT and in selected cases contrast-enhanced MRI. The first therapy's phase provided to deliver high radiation doses within bulky tumour using "balls of dose", called VERTEX, positioned between hypoxic and normoxic tissue following a non-geometric model, delivering a median total dose of 15Gy (range 10-27Gy) in 1-3 fraction. Generally V5 and V3 on GTV were <50% and <65%% respectively. In the second phase a median total dose of 21.7Gy (range 18 – 40,05Gy) was delivered on GTV ± Clinical Target Volume (CTV). With a median follow up of nine months (range 1-23 months) we recorded an 93.5% of clinical response, specifically 46.8% complete response (CR) and 46.7% partial response (PR) has

been observed. Stable disease (SD) and progression disease (PD) were 6.5% and 2.1% respectively. The median Overall Survival was 12 months (range 1-25 months). Toxicities were negligible with no grade ≥ 2 toxicities observed.

Conclusions: The LATTICE_01 approach is feasible and well tolerated with encouraging results in terms of toxicities and clinical outcomes rate. These preliminary results seem to indicate that this kind of therapy could emerge as a therapeutic option for the bulky tumour disease, also potentially without systemic disease.

CO76

PET/CT RADIOMIC FEATURES TO PREDICT CLINICAL OUTCOMES IN LOCALLY ADVANCED PANCREATIC CANCER

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Background: Innovative biomarkers to predict clinical outcomes in pancreatic cancer would be helpful in optimizing personalized treatment approaches. In this study, we aimed to develop PET/CT-based radiomic biomarkers to predict early progression in patients with locally advanced pancreatic cancer (LAPC).

Method: Among one-hundred fourteen patients with LAPC treated at our institution with initial chemotherapy followed by curative chemoradiation (CRT) from July 2013 to March 2022, a secondary analysis with baseline 18F-FDG PET/CT images was conducted in fifty-seven patients. All pre-treatment PET/CT were performed at a single PET/CT Centre. Clinical factors as well as semi-quantitative PET parameters, including standardized uptake value (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG), were also reported. Early progression (EP) was defined temporally as a progression at the first evaluation, at 3 months from the start of treatment. EP was evaluated by CT scan, resulting in a dichotomous label of progression. A 3D Volume of Interest (VOI) was placed over the primary tumour, manually delineated. Three families of hand-crafted features were extracted from the VOIs of each patient's images, from both CT and PET acquisitions, thus quantifying grey intensity and tissue texture. Statistical features consisted of the moments up to the fourth-order of the first-order image histogram, *i.e.*, the mean, the standard deviation, the skewness and the kurtosis. Texture features were derived from the 3D gray-level co-occurrence matrix (GLCM) and from the Local Binary Patterns-TOP (LBP-TOP). The final dataset was then created by adding clinical data from each patient. The predictive pipeline consisted of a feature selection phase followed by a sequence of two cascading decision trees in which the second used the predictions of the first as additional features for sample prediction. In the training phase, this model optimised the binarization threshold for classification to be applied later in the testing phase. The whole system follows a ten fold cross-validation approach. The quality of the proposed model was appraised by means of receiver operating characteristics (ROC) and areas under the ROC curve (AUC).

Results: Given each 3D VOI in the images, we computed the radiomics features, taking into consideration 12 statistical features, 230 textural features (182 GLCM, 48 LBP-TOP) extracted from the images, and adding 15 clinical features. Figure 1 shows the final performance. To the best of our knowledge, this is the first study for feasibility and hypothesis generation of a radiomic strategy to predict early progression in LAPC and our data suggests that a specific signature can be identified (AUC 0.83; prediction accuracy 80.7%).

Conclusions: This model based on clinical and PET/CT radiomic features assessed before treatment can predict the early progression in LAPC patients. It could be a promising pre-treatment, non-invasive, approach that can assist physicians in evaluating the risk of early progression in patients individually, and thus achieving a personalized treatment and better clinical outcomes. The identification of the external validation dataset is actually ongoing.

CO77

HELP OF ARTIFICIAL INTELLIGENCE (AI) IN CLINICAL PRACTICE: PRO & CONS

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Aims: To evaluate performance and clinical utility of auto-contour generated by AI-based software on CT studies.

Methods: The structures, identified on CT scan were contoured manually and by deep-learning based auto-contouring software (Limbus) for adjuvant breast and pelvis brachytherapy (BT) and external beam radiotherapy (ERT) treatment planes. The time of AI auto-contouring and performance of organ at risks (OARs) contours were evaluated respect to manually one in these settings considering that the software was not primary educated for BT treatments.

Results: In our centre we selected 30 patients with breast cancer (13/17 right/left side) treated with interstitial BT or ERT in 20 and 10 cases, respectively. Moreover 30 other patients, underwent to surgery for endometrial cancer, were submitted to adjuvant endocavitary vaginal

BT and pelvic ERT in 24 and 6 cases, respectively. In all CT scan OARs were contoured by AI and then by a single radiation oncologist (RO). Each contour (including manual) was visually evaluated in a blinded test. After examination of AI OARs contouring, a RO (other than the reference one) assigned a score proportional to the degree of correction needed for clinical acceptability: 0 (no corrections), 1 (minor corrections), 2 (major corrections). The median time of OARs auto-contouring in all cases was 2 minutes. On the contrary, in case of manual contouring the time was 15-20 and 30 minutes for right breast, left breast cancer and endometrial cancer, respectively. The median time saved with AI was about 90%. About performance of OARs volumes AI contours have a high degree of clinical acceptability (score 0) in case of thorax and pelvis ERT. For thorax BT plans, AI contours have medium degree of clinical acceptability (score 1) and high degree (score 0) for breast and others thorax OARs, respectively. Indeed, for pelvis BT plans, AI contours have low degree of clinical acceptability (score 2) for rectum and bladder volumes and high degree (score 0) for others pelvis OARs. Probably these last results are related to interference of BT catheters or vaginal applicator. In BT planes, AI breast, rectum and bladder volumes were corrected by RO in median 12 minutes.

Conclusions: AI as auto-contouring tool is a valid and safety help for clinical practice of ROs, it allows you to reduce contouring-time. Auto-contours have a quality comparable to manual contours, however it cannot completely replace the physician who must supervision always AI work. The observed differences in the software performances could be due to different training levels, particularly for BT treatment planes. We look forward to training AI to obtain an optimal auto-contouring tool also with BT applicators.

CO78

BASAL CELL CARCINOMA OF THE SKIN OF THE HEAD: A COMPLEX CLINICAL CASE TREATED BY EXTERNAL BEAM RADIOTHERAPY

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Aims: Basal cell carcinoma (BCC) accounts for 80%-90% of all cases of skin cancer and is the most frequently occurring form of cancer in humans. High-risk (HR) BCC denotes primary or relapsed tumors with a significant risk of further relapse after local treatment.[1] Surgery and external beam radiotherapy (EBRT) are the treatment of choice for most patients with HR lesions.[2] Since HR BCC arises more frequently in the head and neck, the tumor may infiltrate the eye, nose, facial bones, skull or brain and result in significant symptoms and complications.[3] The treatment options for patients in which surgery is technically unfeasible is generally sequential chemoradiation with systemic therapy Cisplatin based.[4] Another treatment option is Vismodegib, an oral small molecule inhibitor of the Hedgehog pathway, abnormal activation of which is associated with BCC. This drug is indicated for the treatment of adults with metastatic BCC or locally-advanced BCC that has recurred following surgery, generally not candidates for further surgery or EBRT][5]. We present the case report of a patient with a destructive BCC of the skin of the vertex and of the right temporo zygomatic region treated by EBRT in our Institution.

Methods: A 90 years-old man in good performance status (PS) was addressed to our Radiotherapy Center in May 2021. He had multiples surgical resection of different cutaneous lesions (head skin in the left temporal zone in 1987, left auricle in 1999, 2000 and 2003, skin of the right thorax in 2001, head skin in right temporo parietal region in 2012), all classified as BCC. In 2017 he started biologic therapy with Vismodegib for BCC relapse at different sites of the head, in particular for a large (about 8 cm) ulcerated area of the vertex and another (about 4 cm) lesion in the right temporal region. This treatment was maintained for 3 years, with stability of the lesions. In 2021, a progression disease with major excavation of the lesions and local pain appeared. The total body computed tomography didn't show metastatic disease.

Results: A treatment by EBRT on the two sites was planified and realised from the 10th June 2021 to the 14th July 2021. The lesion of the right temporo zygomatic region was treated by an electrons field of 9MeV energy with a bolus of 0.5 cm in depth (total dose (DT): 50 Gy in 20 sessions), and the ulcerated lesion of the vertex was treated by intensity modulated radiation therapy (IMRT) (DT of 50 Gy in 20 sessions), with six photons fields (energy 6 MV) to avoid the placement of a bolus on the ulcerated skin and to limit the physical inhomogeneities lied to the irregular surface of the large lesion. 95% of the temporo zygomatic lesion treated by electrons beam was covered by the isodose of 90%; while 95% of the vertex lesion treated by IMRT was covered by the isodose of 94%. No acute toxicity was reported, except a grade 1 erithema (according to CTCAE v4 scale) in the treated areas. At one year from the EBRT treatment, patient is alive, in good PS and with absence of pain on the treated BCC lesions.

Conclusions: Management of locally advanced BCC relapsed after prior surgery is complex. EBRT represents an useful therapeutic weapon even for large lesions located in irregular areas, which nowadays can be successfully treated by modern radiotherapy techniques like IMRT.

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CO79

USE OF RADIOTHERAPY FOR NON MELANOMA SKIN CANCER (NMSK) CURATIVE TREATMENT: THE AIRO CAMPANIA EXPERIENCE

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Aims: Radiotherapy (RT) represents a therapeutic option for the exclusive treatment of non-melanoma skin cancers (NMSC). RT is reserved for patients who are inoperable due to refusal, poor clinical condition or surgical infeasibility. Different techniques and fractionations are used depending on characteristics of the patients and lesions to treat according to clinical judgement. The aim of this study is to present data from NMSC patients treated in seven high volume RT centres in Campania.

Methods: Seven Centres from the AIRO Campania group decided to participate in a retrospective data collection of patients with NMSC. Clinical and dosimetric data and acute toxicity information according to the Common Terminology Criteria for Adverse Events (CTCAE) 5.0 scale were collected. Treatment response, considered ad complete response (CR), partial response (PR), stable disease (SD) and progression disease (PD) was assessed clinically according to Response Evaluation Criteria in Solid Tumours (RECIST) criteria.

Results: A total of 250 patients, median age 80 (range 42-99) years treated with exclusive RT from January 2019 to March 2022 were included in our analysis. Patients characteristics are reported in Table 1. Interestingly, many physicians preferred hypofractionated schedule due to age and to COVID19 period. In particular, the most frequently used fractionation (27.6%) was 40Gy delivered in 5 fractions. Out of 147 (58,6%) patients whose acute toxicity data were available, 73,5% of patients developed G1-G2 erythema and only 2,04% developed G3 moist desquamation. Nine patients (3,6%) didn't ended scheduled treatment but only 3 of them due to G≥3 toxicity. Of 157 (62.8%) patients whose data were available, the response to the first clinical re-evaluation within 3 months after the end of RT showed CR in 40 (25.48%), PR in 100 (63.69%) and SD in 3 (1.91%) patients, achieving a local disease control of 91%.

Conclusions: Radiation therapy is a cornerstone in the treatment of skin cancers with exclusive purpose. This multicenter embryonic study confirms how it is a safe and effective therapeutic modality with high rates of local disease control and low toxicity rates. This retrospective collection can be the basis for future prospective studies.

CO80

DEEP LEARNING SEGMENTATION IN RADIOTHERAPY: ANALYSIS OF CLINICAL IMPLEMENTATION

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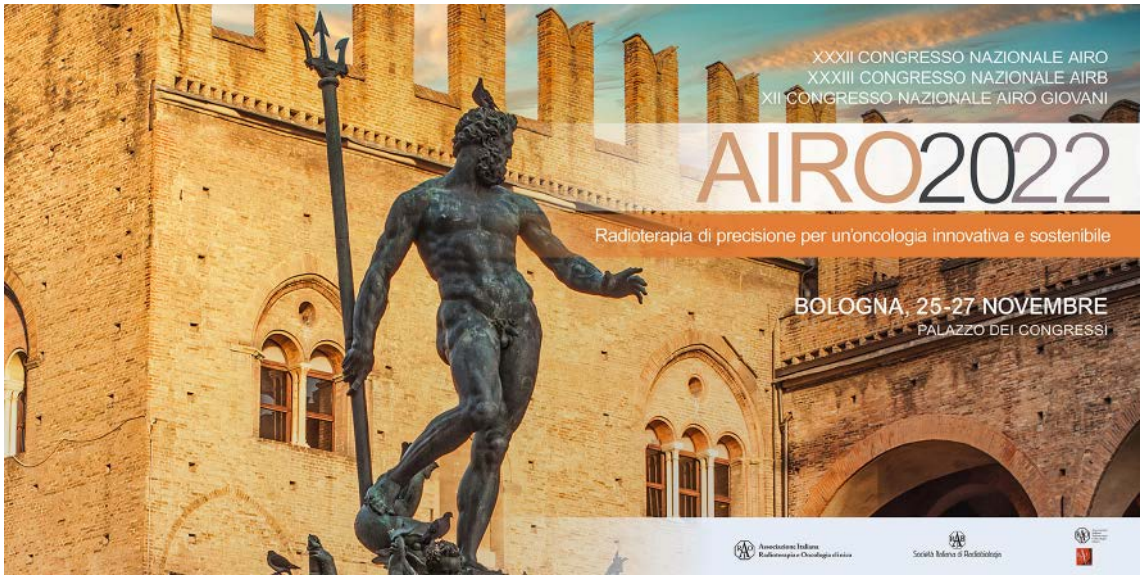
Aims: Accurate contouring of Organ At Risk (OAR) is an important key of treatment planning in radiation oncology; generally the segmentation of normal tissues is manually performed by clinical staff. This approach is time-consuming and makes the procedure subject to a high degree of variability, often representing a bottleneck in the planning workflow. The purpose of our study is to investigate in our institution the clinical implementation of a specific deep learning based auto contour commercial software for four specific disease sites: head and neck (oropharynx), prostate, breast and rectum.

Methods: The commercial deep learning based autosegmentation software, Limbus Contour (LC), has been implemented in our institution. We choose for each disease site three patients treated in our center in 2021. The same TC acquisitions were contoured by LC. The LC structure set was later duplicated and reviewed by the competent Radiation Oncologist (RO) and, if necessary, the contours have been modified. The time taken by RO to perform the manual contour for each TC scan was recorded. The overall duration of contouring using LC (LC contouring + RO review) was compared to the time required to perform manual contouring. The manually contoured structures (MC) were compared with the LC ones by means of volume variation, Dice Similarity Coefficient (DSC) and shift of the center of mass.

Results: The maximum time saving, both absolute and relative, was obtained for the H&N (80 minutes and 65%, respectively). The minimum changes, both absolute and relative, were found for rectum (3 minutes and 17%, respectively). The OAR with the minimum average percentage variation in volume (1%) is lung; the structures with the greatest percentage variation are bowel and oral

cavity, with mean percentage variations of 65% and 32%. The lowest values of the DSC were found for inner ear, while the best results were found for lungs. The lowest values of the three-dimensional displacement of the center of mass were found for lungs, with values close to 0 cm. The greatest displacement occurred for bowel, with a value equal to 2.4 cm.

Conclusions: LC can significantly reduce the time required for contouring and simplify the workflow leading to treatment planning. Its implementation also allows to reduce interobserver variability and improve the interpretation of radiological anatomy.



Discussed Poster

DP01

A PATTERN OF CARE REPORT ON THE MANAGEMENT OF PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE ANUS – A STUDY BY THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO) GASTROINTESTINAL TUMORS STUDY GROUP

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Aims: Diagnosis and therapy of squamous cell carcinoma of the anus may vary importantly in daily clinical practice, even if international guidelines are available. We conducted a pattern-of-care survey to assess the management of patients with anal cancer in Italy.

Materials and Method: The project was developed within the Study Group for Gastrointestinal Tumors of AIRO, whose Directive Council acted as a steering committee. An external panel of radiation oncologists with a specific expertise in the management of anal cancer provided suggestions and comments. Face validity, together with the content, wording and general flow of the survey was internally evaluated. Participants were invited to participate voluntarily (February-March 2021) via email, after identification as members of AIRO. The invitation was sent by the Secretariat of AIRO. One radiation oncologist per center was allowed to participate in the survey. Demographics and professional information useful for

stratification were collected. The questionnaire consisted of 38 questions, some of them allowing for multiple answers and comments, and covering diagnosis and treatment of SCC of the anal canal and margin Statistical analysis was provided by www.surveymonkey.com and included a description of all variables. Responses were tabulated, and the percentage values reported. The survey was compliant with the CHERRIES guidelines for reporting results of internet e-surveys.

Table 1. Radiotherapy dose prescription and delivery.

Imaging for GTV Definition (Both Primary Tumor and Lymph nodes) (Multiple Answers Allowed)	N (%)
Planning CT	8 (13.8)
Pelvic CT	19 (32.8)
Pelvic MRI	52 (89.7)
^{18}FDG-PET	45 (77.6)
RT delivery technique (multiple answers allowed)	
3DCRT	0 (0)
IMRT	10 (17.2)
Volumetric IMRT	52 (89.7)
Tomotherapy	12 (20.7)
MRgRT	0 (0)
Primary tumor boost (multiple answers allowed)	
EBRT-Sequential boost	26 (44.8)
EBRT-SIB	49 (84.5)
EBRT-Electrons	2 (3.4)
Endocavitary or Contact BRT	3 (5.2)
Interstitial BRT	4 (6.9)
Treatment after local excision for T1N0 tumor with risk factors	
Exclusive RT with definitive dose	21 (36.2)
RT-CHT with RT dose de-escalation	13 (22.4)
RT-CHT with definitive RT dose	17 (29.3)
RT with dose de-escalation	2 (3.5)
Others	5 (8.6)
RT dose to primary tumor GTV for T1–T2 tumors (dose range) (multiple answers allowed)	
45–45.9 Gy	2 (3.5)
50–50.4 Gy	27 (46.5)
54–55 Gy	34 (58.6)
56–59.4 Gy	7 (12.1)
≥60 Gy	4 (6.9)
RT dose to primary tumor GTV for T3–T4 tumors (dose range) (multiple answers allowed)	
53 Gy	1 (1.7)
54–55-5 Gy	36 (62.1)
56–59.4 Gy	19 (32.8)
≥60 Gy	13 (22.4)
Dose to elective volumes (multiple answers allowed)	
30.6 Gy	1 (1.7)
36–37.5 Gy	2 (3.5)
42–42.5 Gy	5 (8.6)
45–45.9 Gy	55 (94.8)
49.5–50.4 Gy	11 (18.9)
>54 Gy	3 (5.2)
Dose to involved nodes (sized < 3 cm) (multiple answers allowed)	
40 Gy	1 (1.7)
45 Gy	1 (1.7)
50–51 Gy	34 (58.6)
52–53.2 Gy	6 (10.3)
54–56 Gy	19 (32.8)
59–59.4 Gy	2 (3.5)
≥ 60 Gy	4 (6.9)
Dose to involved nodes (sized > 3 cm) (multiple answers allowed)	
45 Gy	1 (1.7)
50–50.4 Gy	4 (6.9)
52–52.5 Gy	2 (3.5)
54–56 Gy	50 (86.2)
59–59.4 Gy	3 (5.2)
≥60 Gy	5 (8.6)

Legend: N: number; GTV: gross tumor volume; RT: radiotherapy; CT: computed tomography; MRI: magnetic resonance imaging; ^{18}FDG-PET: fluorodeoxyglucose positron emission tomography; 3DCRT: 3-dimensional conformal radiotherapy; IMRT: intensity modulated radiotherapy; MRgRT: magnetic resonance guided radiotherapy; EBRT: external beam radiotherapy; SIB: simultaneous integrated boost; BRT: brachytherapy; CHT: chemotherapy.

Results: We analysed 58 questionnaires. Most of the respondents works in public and/or university hospitals (75.8%), in northern Italy (65.5%). The majority (88.0%) treats less than 20 patients/year. Common examinations for diagnosis and staging are anorectal endoscopy (84.5%), computed tomography scan (86.2%) and pelvic magnetic resonance imaging (MRI) (96.5%). The most frequently prescribed dose to primary tumor is 50-54 Gy (46.5-58.6%) for early-stage disease and 54-59.4 Gy (62.1-32.8%) for locally-advanced cases. Elective volumes are prescribed around 45 Gy (94.8%). Most participants use volumetric intensity modulated radiotherapy (89.7%) and a simultaneous integrated boost (84.5%). Concurrent radiotherapy, 5-fluorouracil and mitomicin is considered standard of care (70.6%). Capecitabine is less frequently used (34.4%). Induction chemotherapy is an option for extensive localized disease (65.5%). Consolidation chemotherapy is rarely used (18.9%). Response evaluation is done at 26-30 weeks (63.9%), with a pelvic MRI (91.4%). Follow up is generally run by the multidisciplinary tumor board (62.1%).

Conclusions: Generally, a good level of agreement was found in Italy with respect to diagnosis and management of anal cancer. Differences were observed for radiotherapy dose prescription, calling for a consensus to harmonize treatment strategies.

DP02

HIGH DOSE PROTON AND PHOTON-BASED RADIATION THERAPY FOR LIVER LESIONS: A MULTI-INSTITUTIONAL DOSIMETRIC COMPARISON WITH A CLINICAL PERSPECTIVE

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Introduction: Stereotactic radiotherapy (SRT) and Proton therapy (PT) has revolutionized the role of radiation oncologist in the management of liver lesions. Limited clinical data of comparison between techniques are available.

Methods: Primary endpoint was to assess and compare healthy liver sparing of Rt techniques. The biological effective dose (BED) was calculated to compare different fractionations and doses. rV18 Gy represents the area of healthy liver receiving less than 18 Gy in 3 fractions. The linear quadratic model was used to calculate the BED for 18 Gy (39.6 Gy in 3 fractions). We calculated from this value of BED the corresponding value of the isotoxic dose in 15 fractions and 5 fractions that resulted 28.5 Gy and 21.5 Gy. For 15 and 5 fractions, respectively. A biologic MRI-based model was exploited to confirm such results.

A so-called Fall-off Volume was defined:

FALL-OFF VOLUME = whole liver - PTV - (rV18 or rV21.5 and rV28 for 3, 5 and 15 fractions)

The result represents the area of the healthy liver receiving 18 Gy (3 fractions), 21.5 Gy (5 fraction) and 28.5 Gy (15 fractions) with photon- or proton-therapy, respectively.

Subsequently, a Fall-off Ratio was defined:
FALL-OFF RATIO = the Fall-off Volume / PTV
Fall-off Ratio express how big is the area of radiation induced liver reaction in relationship to PTV dimension (Figure 1).

Results: 158 Pts for 193 lesions were identified. MRI-based model confirmed the biological consistency for the three isotoxic doses of 18 Gy, 21.5Gy, and 28.5 Gy, demonstrated to be isoeffective in determinate liver damage. We proceded to compute and compare Fall-off ratios. Median fall-off ratio was 0,57 (range 0,1-1,54) for proton, 4.5 (range 0,93 – 16) for Vmat FFF with 5mm jaws, 5 (range 3-9,7) for Cyberknife plans, 6,2 (range 2-24,5) for Vmat FF with 10 mm jaws. Difference emerged in fall-off ratio between proton and photons (p<0,001). Between photons, a significantly better fall-off ratio was found for Vmat FFF technique with 5mm Jaws treatment compared to Vmat FF technique with 10mm jaws (p=0,013). No difference between Vmat FFF with 5mm jaws and Cyberknife technique was found.

Conclusions: Our clinical model confirmed that proton therapy spares more healthy liver compared to photon srt. Robotic srt and v-mat fff with 5mm jaws spare more healthy liver than v-mat ff with 10 mm jaws. Fall-off ratio could be useful to measure and compare quality of plans in terms of fall off in clinical practice also in heterogeneous clinical situations.

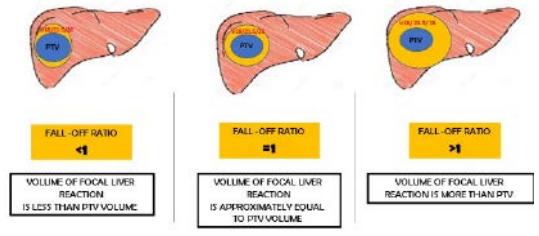

Figure 1.

DP03

ANAL SQUAMOUS CELL CARCINOMA: IMPACT OF RADIOCHEMOTHERAPY EVOLUTION OVER YEARS AND AN EXPLORATIVE ANALYSIS OF MRI PREDICTION OF TUMOR RESPONSE IN A MONO-INSTITUTIONAL SERIES OF 131 PATIENTS

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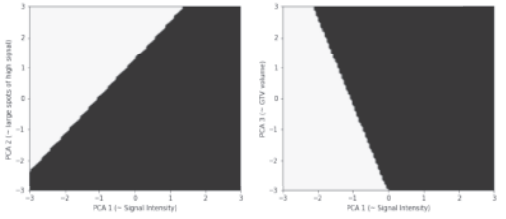
Introduction: Radiochemotherapy (RTCHT) for the treatment of anal squamous cell carcinoma (ASCC) evolved dramatically. Despite most patients presents fair outcomes, predictors of poor tumor response are lacking; Our study describes pattern of treatment evolution in a high-volume centre, exploring the possible role of pre-treatment MRI in predicting tumor response.

Patients and Methods: ASCC stage I-III treated with 3D conformal radiotherapy or IMRT were included. Study endpoints were freedom from locoregional recurrence (FFLR), colostomy free survival (CFS), freedom from distant metastasis (FFDM), overall survival (OS), acute and late toxicity. An exploratory analysis was performed to identify possible predictors of tumor response to radiochemotherapy, exploiting all the available pre-treatment MRI and performing Principal Components Analysis (PCA). PCA components were fitted to classify loco-regional recurrence using a Support Vector Machine (SVM) as machine learning classifier. Feature extraction and data analysis were performed in Python ™ and SPSS® v.26.0 software (IBM®).



RESULTS OF THE 3-COMPONENT SVM CLASSIFICATION. WHITE AREA IS RELAPSE, BLACK IS NO-RELAPSE. PCA COMPONENT ARE NORMALIZED SUCH THAT DATA HAVE ZERO MEAN AND VARIANCE ONE. ON THE LEFT CLASSIFICATION BASED ON SI VS LANGLE, ON THE RIGHT BASED ON SI VS GTV VOLUME. CLASSIFICATION BASED ON LANGLE VS GTV VOLUME IS REDUNDANT AND NOT SHOWN FOR SIMPLICITY.

Figure 1.

Results: 131 patients were identified. After a median FU of 52 months, 83 pts (63,4%) were alive. 35 pts (26,7%) experienced a locoregional failure. Five years FFLR, CFS, DMFS, OS resulted 72,3%, 80,1%, 74,5% and 64,6%. At Multivariate analysis, 2D IGRT predicted poorer FFLR, OS and CFS (HR 4.5, 4.1, 5.6, respectively); moreover, 3DcRT was associated with poorer OS and CFS (HR 3.1, 6.6, respectively). IMRT reduced severe acute gastro-intestinal (GI) and severe skin acute toxicity. Thirty-one pts presented an available diagnostic MRI. PCA applied to T2 images shows that the first component (PCA1) is enough to explains more than 99% of variance, and Total Energy is the main contributor to this

component (98%). SVM classifier had the best fitting with 2 to 3 components, the main contributor to PCA 2 being Gray Level Size Zone Matrix's Large Area High Grey Level Emphasis (GLSZM's LAHGLE) (99%), and GTV volume (97%) to PCA3. Figure 1 shows our best classifier using 3 PCA components

Conclusions: IMRT and daily 3D image guidance may to be considered standard of care in the management of ASCC. A combination of three pre-treatment MRI parameters such as Signal Intensity (SI), Gray Level Size Zone Matrix's Large Area High Grey Level Emphasis (GLSZM's LAHGLE), and GTV volume could be integrated in risk stratification to identify candidates for RT dose-escalation to be enrolled in clinical trials.

DP04

OBSERVATIONAL MULTICENTER ITALIAN STUDY ON VULVAR CANCER EXCLUSIVE RADIOTHERAPY (OLDLADY 1.1): A COOPERATION AMONG AIRO GYN, MITO AND MANGO GROUPS

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Aims: Vulvar cancer is a relatively uncommon type of gynaecologic cancer. The aim of this study was to define efficacy and safety of exclusive radiotherapy (RT) +/- chemotherapy in a large, real-world data set of patients with vulvar cancer (VC).

Methods: Data was obtained retrospectively from VC patients treated with RT in seven Italian Radiation Oncology Centers between January 2010 and December 2021. All patients underwent radiotherapy (45 Gy external-beam radiotherapy/1.8 Gy per fraction) +/- chemotherapy on the pelvic area plus overdosage on gross tumor volume (GTV) and positive nodes. The primary study end-point was the local control (LC), secondary endpoints were metastases free survival (MFS), overall survival (OS), and the rate and severity of acute toxicities.

Results: A total of 80 patients were included in the analysis, with a median age of 73.5 years (range 32-89). Forty patients received a total dose ≥70Gy and 40 patients a total dose <70Gy (range 60-66Gy) on the GTV. On positive nodes, 44 patients got a total dose > 65 Gy and 27 patients received a total dose ranging between 45-60 Gy. Nine, twelve, forty five and fourteen patients were Stage I, II, III and IV, respectively. Sixty-six patients (57.5%) and sixty (75%), respectively, achieved tumor and nodal full remission. With a median follow-up of 11 months (range 1-114 months), the 24-month actuarial LC rate, MFS and OS were 49%, 79.8%, and 53.8%, respectively. Acute toxicity was registered in 69 patients, with sixteen and ten cases of proctitis G1 and G2, respectively; twelve, eighteen, and one case of cystitis G1, G2, and G3; and five, forty-one, and twenty cases of skin toxicity G1, G2, and G3, respectively. Three and five patients, respectively, had lymphedema G1 and G2.

Conclusions: For patients with locally advanced vulvar cancer, RT should be considered the first line of treatment; however, due to mixed outcomes, further research is needed to establish the best radiation treatment for these patients.

DP05

EFFICACY AND SAFETY OF INTENSITY MODULATED RADIATION THERAPY IN VULVAR CANCER: DISAPPOINTING RESULTS FROM AN OBSERVATIONAL SINGLE-CENTER STUDY

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Aims: Radiotherapy (RT) of vulvar cancer (VC) is a treatment option in both patients with advanced disease and in the adjuvant setting. Intensity Modulated RT (IMRT) and Volumetric Modulated Arc Therapy (VMAT) enable more conformal dose distribution and the delivery of higher doses to the target and lower doses to organs at

risk. Here we report the results from an observational study on clinical outcome and toxicity in VC patients treated in our center with IMRT/VMAT(VulCan study, code CE 312/2019/Oss/AOUBo).

Methods: VC patients who underwent adjuvant or definitive IMRT or VMAT in our institution were included in this analysis. Toxicity, local control (LC), overall survival (OS), progression free survival and pattern of recurrence were evaluated.

Results: Forty-one patients were included. Median age was 77 years (range 46-93). Most patients were treated with IMRT, from 2016 to 2021. Adjuvant RT was delivered in 41.5% patients and definitive RT in 58.5%. The delivered RT dose to the vulva in the adjuvant and definitive settings ranged between 39.6–65 Gy and 32.4-66 Gy, respectively, while the dose to the inguinal nodes was 45-65 Gy and 32.4-66 Gy, respectively. Moreover, 48.8% of patients were treated for locally recurrent VC. Concurrent chemotherapy was used in 18 patients (44.0%). Most patients showed grade 2 (22%) or 3 (73.2%) skin acute toxicitywhile gastrointestinal and genitourinary toxicity affected fewer patients and with lower grades of severity. Treatment was not completed in 4.9% of patients. One- and 2-year LC was 68.3% and 55.7%, respectively, with better results in the adjuvant setting (two-year LC 67.9%). Two-year OS was52.5 and 27.4% in patients treated with adjuvant and definitive RT, respectively (Figure 1), with a statistically significant difference (p 0.019).

Conclusions: VC is a rare disease and most of available evidence is based on retrospective studies. Clinical outcome was not satisfactory in our patients, especially in those treated for local recurrence after previous surgery. Despite IMRT allows improved dose distribution, our data suggests that in an elderly population it is difficult to complete treatment without interruptions and to achieve satisfactory clinical outcomes. Moreover, skin toxicity remains an important limitation to deliver a high RT dose.

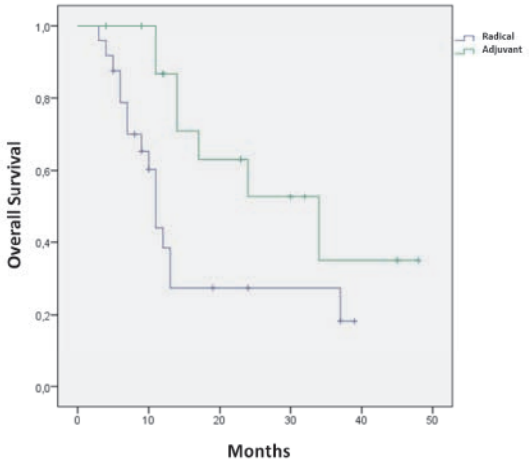

Figure 1. Actuarial overall survival (adjuvant versus radical radiotherapy).

DP06

COMPARISON OF TRANS-VAGINAL ULTRASOUND (TVUS) AND MAGNETIC RESONANCE IMAGING (MRI) FOR THE EVALUATION OF TUMOUR VOLUME IN LOCALLY ADVANCED CERVICAL CANCER TREATED WITH EXTERNAL BEAM RADIOTHERAPY (EBRT) AND BRACHYTHERAPY BOOST: PRELIMINARY ANALYSIS

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Aims: The aim of this study was to perform a blinded comparison between TVUS and MRI for the assessment of tumour volume at diagnosis and before the first boost brachytherapy (BT) application (without applicator in place) in a small cohort of 10 locally advanced cervical cancer patients (pts).

Table 1.

AGE	
Median	53,2 years
Range	47-60 years
HISTOLOGY	
Squamous cell	9
Adenocarcinoma	0
Clear cell	1
FIGO stage	
I B3	1
II B	6
III C1	3

Table 2.

Median Volumes (cm³)			
	MRI	US	p (WILCOXON TEST)
Post-EBRT (sample size=9)	2,49	1,44	0,4258
Pre-EBRT (sample size=10)	26,015	19,15	0,0645

Method: Ten consecutive biopsy-proven cervical cancer patients (pts) referred to our department were prospectively included in this analysis. Patient clinical and pathological features are given in Table 1. At diagnosis all pts underwent pelvic MRI and TVUS before receiving pelvic EBRT with concomitant chemotherapy. At the fourth week of treatment, patients underwent clinical re-evaluation with pelvic MRI and TVUS before starting

brachytherapy boost. We measured the tumour volume estimated on each MRI and TVUS study; the volume was calculated by using a rotational ellipsoid based on the three axis (CC, AP, LL) that was determined by dedicated physicians, radiologists and gynaecologists. The volumes measured on MRI and TVUS images, taken before and after EBRT, were compared. Statistical non parametric Wilcoxon test for paired data was used because the normality test assessed on data showed a non gaussian distribution.

Results: The results of our preliminary analysis are shown in Table 2: no statistically differences between tumour volumes calculated on MRI and TVUS were found (p=0.4258; p=0.0645).

Conclusions: The precondition for a safe and good quality BT treatment is the precise identification of target volumes to elaborate an optimal pre-planning. MRI has demonstrated clear advantages in terms of image quality as it allows the optimal definition of normal peri-cervical soft tissues, tumour extension within the cervix and parametrial infiltration. Additionally, MRI enables 4D volume adaptation following tumour regression during EBRT. However, due to its costs and limited availability, most patients worldwide are precluded from receiving MRI-based BT treatment. Ultrasound (US) has excellent soft tissue resolution, is affordable, and has been used extensively in cervical cancer diagnosis. For all these reasons US is under investigation as a potential alternative to MRI for Image-Guided Adaptive Brachytherapy planning. Based on our very preliminary data, TVUS seems indeed to be potentially useful to evaluate tumour response after EBRT and also to perform BT pre-planning, provided that these findings are confirmed in larger series of pts.

DP07

A COMBINATION OF MRI AND [18F]FDG-PET MEASURES INDEPENDENTLY PREDICTS THE OVERALL SURVIVAL IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER (LACC) TREATED WITH CHEMORADIOTHERAPY

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Aims: The added value of 18F-FDG-PET for staging and treatment planning of locally advanced cervical cancer (LACC) candidates to chemoradiotherapy has been increasingly recognized. However, very few studies compared the prognostic value of different PET-based metrics. Moreover, the added value of FDG PET with respect to clinical and MRI-based measures still need to be clarified. We aimed to evaluate the added value of baseline FDG PET to predict overall survival (OS) in patients with LACC.

Methods: From 2010 and 2019 we retrospectively analyzed 60 patients with LACC treated with EBRT +/- platinum-based chemotherapy plus high dose-rate brachytherapy (HDR-BT). We recorded the following baseline variables: age, FIGO stage, baseline MRI finding like extension of primary lesion (T), lymph nodes (N) number and site, and invasion of parametrium and/or vagina; baseline FDG PET-derived maximum and mean SUV, MTV and TLG for both T and N. All variables were entered in the univariate and multivariate analysis.

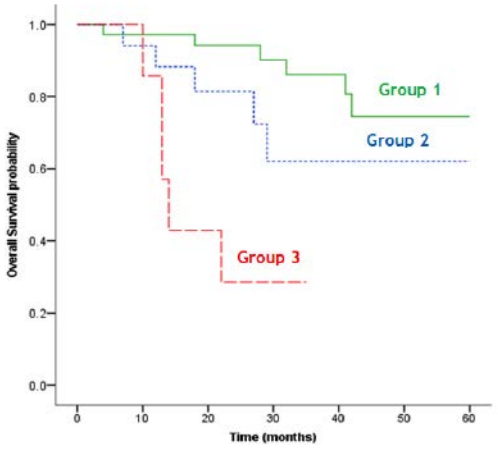

Figure 1.

Results: Mean age of population was 59.2±13.1 years (range 37-90). EBRT was mainly delivered by IMRT helical technique (60% pts). Most used fractionation schedule were EBRT 45 Gy in 25 fr or 50,4 Gy in 28 fr with a median SIB of 57.5 Gy if evidence of parametrial disease or pelvic/LA lymph nodes involvement; BT 28 Gy in 4 fr or 30 Gy in 5 fr. FIGO stage, T TLG and MTV, N SUVmax, TLG and MTV and number of MRI-detected lymph node resulted significant predictors of the OS at univariate analysis. Only MRI-based number and PET-based MTV of lymph nodes were identified as independent predictors of the OS at multivariate analyses (respectively p=0.035 and p=0.042). A post-hoc analysis was performed after binarizing PET and MRI metrics of the N (cut-offs N-MRI>10 and N-MTV≥3.55) and patients were subgrouped based of both cut-offs by a Kaplan-Meier analysis (Figure 1). The groups identified showed a significantly different OS (median duration expressed in months; p=0.004): when both predictors were below both cut-off OS was 53 months (n=36-Group1), when they were above the cut-off OS was 22 months (n=7-Group2); when at least one predictor was above cut-off OS was 42 months (n=17-Group3).

Conclusions: The combination of baseline lymph-node number at MRI and PET-derived N-MTV distinguishes three classes of patients affected by LACC characterized by significantly different OS. Present findings confirm the role of FDG-PET in combination with MRI imaging in staging LACC.

DP08

TUNING OF LEXICOGRAPHIC OPTIMIZATION-BASED PLANNING FOR CERVICAL CANCER: HOW FAR CAN WE GO?

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Aims: Recently, a not yet commercially available fully-automated lexicographic optimization planning system (APS) has been validated for cervical cancer (CC) at our Institution. Constraints and objectives were sequentially optimized by multi-criterial optimization according to an a-priori assigned priority list. This study aimed to investigate the possibility to improve the present APS in terms of organs-at-risk (OARs) sparing and plan deliverability.

Method: Twenty CC plans (50 Gy/25 fx) delivered between November 2019 and July 2021 had been previously automatically re-planned. The first AP version (AP_1) asked for OAR sparing only after an optimal target coverage is obtained. The novel AP_2 approach is different: (1) minimum target coverage, (2) OAR optimization gradual steps, and (3) possible target coverage increase. The main criteria for planning approval were a target coverage of $V_{95\%} > 97\%$ (acceptable>95%), a target $D_{1\%} < 105\%$, a bowel volume receiving more than 45 Gy less than 195 cm^3 (V_{45Gy}<195 cm^3), rectum and bladder spared as much as possible. AP_1 and AP_2 plans were compared in terms of dose-volume constraints and plan complexity, i.e. MUs and modulation degree (MD), performing the Wilcoxon Mann Whitney test (alpha=0.05). Plan deliverability was verified by treatment QA and compared with a local (3%/3mm) gamma analysis.

Results: The AP_2 showed a 1%-increase in PTV $D_{1\%}$ (p=0.002) and a 1%-decrease in $V_{95\%}$ (p>0.05). The plan comparison registered a decrease of -16.4%, -19.0%, -7.45%, -9.9%, and -3.2% in median values for rectum mean dose, rectum $D_{50\%}$, mean bladder dose, bladder $D_{50\%}$, and bowel V_{45Gy}, respectively. A statistical significance has been found in rectum statistics (p<0.02). The AP_2 showed an increased plan complexity (p=0.001): the mean MD was 3.3 ± 0.3 and 4.2 ± 0.6 for AP_1 and AP_2, respectively. The mean MUs were increased, registering 795.5 ± 66.4 and 915.0 ± 93.5 for AP_1 and AP_2, respectively (p=0.001). Nevertheless, the mean gamma index passing rate was comparable for AP_1 and AP_2.

Conclusions: The previous validation showed that APS can strongly reduce the overall planning time by getting plans comparable to manual plans. This further tuning showed the possibility to tune different APSs to promptly answer clinicians' requests: it would be possible to choose, patient by patient, the preferred compromise between DVH and plan complexity. Furthermore, these fast and customizable results suggest exploiting APS in a fast adaptive workflow soon.

DP09

EFFICACY OF RESIDUAL SITE RADIATION THERAPY IN PATIENTS WITH PRIMARY MEDIASTINAL LYMPHOMA WITH DEAUVILLE SCORE 4 FOLLOWING R-CHT

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Aims: To evaluate the efficacy of residual site radiation therapy (RSRT) in term of progression free (PFS) and overall survival (OS) in patients with primary mediastinal lymphoma (PMBCL) with Deauville Score 4 (DS 4) following rituximab and chemotherapy treatment (R-CHT) in a monoinstitutional retrospective study.

Methods: Between 2010 and 2022 we analysed 31 patients with PMBCL with median age of 34 years (range 16-52years). Thirteen patients were females and 18 were males. At the end of R-CHT, patients were evaluated by 18F-fluorodeoxyglucose positron-emission tomography, showing DS4, and were treated with adjuvant RSRT. RT was delivered by Intensity-modulated radiation therapy (IMRT) and three-dimensional conformal RT (3D-CRT). The gross tumor volume (GTV) included morphological mediastinal residual disease after R-CHT. Most patients underwent image-guided radiotherapy (IGRT) using cone-beam computed tomography (CBCT) system as daily pre-treatment imaging. All patients were evaluated every 3 months for the first 2 years and every 6 months afterwards for a period of at least 5 years with clinical and radiological procedures as required. The Kaplan-Meier method was used to calculate survival curve estimates.

Results: All patients received RSRT with a dose of 30 Gy in 15 fractions. Median follow-up was 43 months (range 1-148 months). The median survival was 49 months (range 8-155 months) and 10-years OS was 100%. 1 year and 5 years PFS was 96.6% and 91.5%

respectively. Patients with progressive disease have been treated with high-dose chemotherapy (HDC) and/or autologous stem cell transplant (auto-SCT). Conclusion: RSRT in patients with PMBCL treated with ICHT and DS 4 did not impact unfavourably on patients survival.

DP10

INTERNAL GUIDELINES TO REDUCE THE LYMPH NODE INTER/INTRA-OBSERVER VARIABILITY FOR TOTAL MARROW AND LYMPH NODE IRRADIATION

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Aims: Total Marrow/Lymph node Irradiation (TMI/TMLI) is a modulated radiotherapy technique that targets bone marrow and eventually, lymphatic system and spleen, prior to stem cell or bone marrow transplantation, while spares the high dose from organs at risk. The TMI/TMLI target includes the whole bones, lymph-node system, and spleen. In particular, the accurate lymph-node chains delineation is fundamental to provide correct delivery. We evaluated the impact of the introduction of internal contouring guidelines (GL) for reducing the lymph-node clinical target volume (CTV_LN) inter and intra-variability.

Methods: Since 2010, 114 patients were treated in our center using VMAT. Ten patients were randomly selected from the internal database. CTV_LN was re-contoured by a single expert radiation oncologist according to the new GL (CTV_LN_GL_RO1) and compared to the previous CTV_LN_Old. Ten patients were prospectively contoured by RO1 following the GL. Six of these were further contoured by a second radiation oncologist (CTV_LN_GL_RO2) to check the inter-observer variability, while four were re-contoured by RO1 at least two months later to check the contouring intra-observer variability (CTV_LN_GL_RO1b). All CTV_LNs were splitted in four regions for a detailed analysis: H&N, Thoracic, Abdominal, and Pelvic areas. Dice similarity coefficient (DSC) was calculated for all paired contours. Planning target volume (PTV_LN) was generated adding an isotropic margin of 5 mm to CTV_LN. The TMI/TMLI plans were optimized starting from PTV_LN_RO1 and the volume received by the 95% of the prescription dose (V95%) were computed for the all contours to assess the target coverage and guidelines consistency.

Results: Median CTV and total planning target volume (PTV_tot=margin to (CTV_LN+bones+spleen)) were, respectively, 1.7 l and 16.5 l. A total of 200 target volumes were considered. The mean DSC comparisons were 0.82±0.08, 0.86±0.08, and 0.97±0.02 for, CTV_LN_GL_RO1 vs., respectively, CTV_LN_Old, CTV_LN_GL_RO2, and CTV_LN_GL_RO1b. The largest and lowest differences were observed in, respectively, H&N and abdomen regions. Mean differences between V95% were 4.8±4.7%, 0.3±0.5% and 0.1±0.1%, for the same couples.

Conclusions: This study revealed the CTV-to-PTV margins to be safe, even if relatively low DSCs were observed. The introduction of GL increased the intra and inter CTV dose coverage that could support the reduction of margins in future TMI/TMLI treatments.

DP11

CLINICAL AND SUBCLINICAL CARDIAC EVENTS IN PEDIATRIC HODGKIN LYMPHOMA (HL) PATIENTS TREATED WITH MEDIASTINAL RADIATION THERAPY (RT): HEART DOSE EVALUATION

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Aims: To analyze cardiac events (CE) and doses received by heart and cardiac substructures (CS) in pediatric HL patients (pts) treated with mediastinal RT, by means of a cardiac segmentation process.

Methods: Sixteen consecutive pts affected by classic HL were treated from 2009 to 2017 according to AIEOP LH-2004 protocol. In the current study, 12pts (mean age 14 yrs, range 8-18) were analyzed (Figure 1), while 4 were excluded (disease far from the heart). For cardiac segmentation, deformable image registration was obtained to adapt organs at risk between diagnostic contrast scan and RT simulation CT. The following CS were contoured: right and left atrium and ventricle, mitral and tricuspid valves, left main, left anterior descending, left circumflex and right coronary arteries. CE, PTV coverage (V90, V95, V107%), doses to CS (Dmax, Dmean) were analyzed.

Results: Pts were divided into 2 therapeutic groups (GR): GR2 (5pts) received 4 COPP/ABV + RT (3pts 14,4Gy because complete response (CR), two pts 2 cycles of IEP (Ifosfamide-Etoposide-Prednisone) +25,2Gy because partial response (PR); two GR2 pts irradiated also

subdiaphragmatic site with 14.4Gy (1 irradiated spleen); GR3 (7pts) received 4 COPP/ABV, among these, 6 received 2 further COPP/ABV+RT because initial CR (3pts 25.2Gy and the other three 14.4Gy). One GR3 pt received 2 cycles of IEP for PR + 25,2Gy + 3.60Gy boost on the sternum. Among the 7 GR3 pts, 4 irradiated also subdiaphragmatic site (2pts 25.2Gy and other two 14.4 on spleen). PTV coverage was V90% 97, V95% 90, V107% 1,14 %; Mean heart dose 6,7Gy; Mean left ventricle (LV) dose 5,45Gy. Follow-up (FU) time of 9.2yrs: all pts were in remission and underwent a cardiological evaluation (timing established by the p). During the FU 4pts (33%) presented CE (reduction of LV function and hypokinetic dilated myocardiopathy between 4 and 7yrs after RT) which required drug treatment (ACE inhibitors and B-blockers). Two patients presented a subclinical CE (reduction in LV global longitudinal strain, no therapy). Analysis of the doses received by the whole heart and by CS showed that in pts who had a clinical or subclinical CE, the mean heart dose (7.5 vs 6.4Gy), the mean and max LV dose (7 vs 4Gy and 18 vs 16Gy) and the max arteries dose were higher than in pts with no CE (Figure 1).

Conclusions: Pediatric HL survivors represent a group of pts at high risk for clinical and subclinical CE: long-term cardiac surveillance is mandatory to prevent major CE.

Table 1.

Demographics HL patients (No 12)	
Age (years)	**No. patients (12)**
Median (range)	14 (8-18)
Gender	
Female	7 (58%)
Male	5 (41%)
Familiarity for CVD	
IMA	1 (8%)
Hypertension	4 (33%)
Histology	
Nodular sclerosis	9 (75%)
Mixed cellularity	2 (16%)
Lymphocyte predominant	1 (8%)
Site of primary tumor	
Up	6 (50%)
UP and Down	6 (50%)
Lung	3 (25%)
Spleen	5 (42%)
Stage	
II	6 (50%)
III	4 (33%)
IV	2 (16%)
B symptom	
Yes	5 (7%)
No	7 (58%)
Mediastinal bulky	
Yes	5 (42%)
No	7 (58%)
Diagnostic exams	
CT TB scan	12 (100%)
PET scan	12 (100%)
Electrocardiogram	12 (100%)
Echocardiogram	12 (100%)
Therapeutic Group	
II	**5 (42%)**
III	**7 (58%)**
RT technique	
IMRT butterfly	1 (8%)
3DCRT	11 (92%)

CARDIAC SUBSTRUCTURES	CARDIOVASCULAR EVENT: 1 EVENT, 2 NO EVENT	Dose (Gy)
HEART MAX	1	18,1660
	2	20,0200
HEART MEAN	1	7,5360
	2	6,4500
RIGHT VENTRICLE MAX	1	16,5120
	2	17,7900
RIGHT VENTRICLE MEAN	1	4,9840
	2	5,0917
LEFT VENTRICLE MAX	1	17,6860
	2	16,5285
LEFT VENTRICLE MEAN	1	6,9800
	2	4,5533
LEFT ATRIUM MAX	1	15,970
	2	19,053
LEFT ATRIUM MEAN	1	9,7100
	2	13,4600
RIGHT ATRIUM MAX	1	18,4800
	2	19,3400
RIGHT ATRIUM MEAN	1	9,6740
	2	7,5083
CIRCUMFLEX ARTERY MAX	1	18,1600
	2	17,6493
LEF MAIN ARTERY MAX	1	18,5760
	2	17,9433
RIGHT CORONARY ARTERY MAX	1	17,2200
	2	15,0800
LEF ANTERIOR DESCENDING ARTERY MAX	1	18,5220
	2	15,6717
TRICUSPID VALVE MAX	1	8,4200
	2	9,0383
MITRAL VALVE MAX	1	7,5660
	2	8,8250

DP12

RADIOTHERAPY FOR ELDERLY PATIENTS WITH CERVIX CANCER: FEASIBILITY AND OUTCOME OF CURATIVE TREATMENT

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Aims: Elderly patients with carcinoma cervix (E-CC) are a challenging group to treat. We retrospectively evaluated at our institute the survival outcome and safety of radiotherapy (RT) with or without chemotherapy (CT) in this subset of patients.

Method: Forty-one elderly patients (median 78 years, range 69-89) consecutively referred for curative radiotherapy between July 2008 and March 2020 were evaluated. All the patients were treated with definitive radiotherapy (22 VMAT, 19 conformal 3D), 38 of them receiving external beam and intracavitary brachytherapy (ICBT) boost; 3 patients receiving external beam boost. Twenty-one patients (51.2%) received concurrent chemotherapy using weekly cisplatin. Median total dose for EBRT and ICBT was 50.4 Gy (Range:41.4-60.9 Gy) and 24 Gy (Range:10-30), respectively. Cox multivariate analysis was used to investigate the association between the survival time of and possible predictive factors.

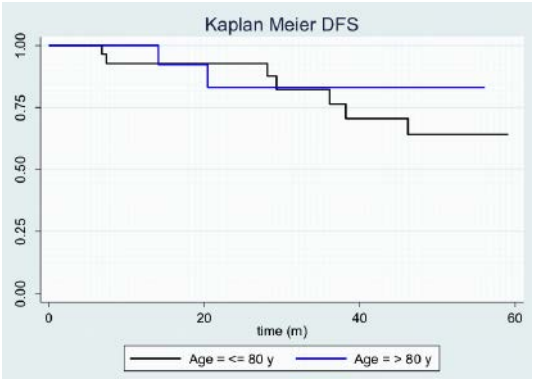

Figure 1.

Results: Thirty-three patients (80.5%) had squamous cell carcinoma, 7 had adenocarcinoma (17%) and one neuroendocrine cancer. Seventeen patients had FIGO IIB stage, 13 had IB1-IIA stage, 11 had III/IVA stage. Median follow-up period was 40.1 months (range 3.7-116.6). All the patients completed the treatment. No grade 3 acute and late toxicity was observed. Nine patients experienced recurrence (local: 4; para-aortic lymph node: 1; distant: 4). Twenty-one patients died during the follow-up period, 6 patients due to the primary disease, 15 for other causes (5 unknown). All patients aged > 80 years died for other causes. Overall 5-year survival and disease-specific survival (OS and DSS) rates for all patients were 82.8% and 67.9%, respectively. By Cox multivariate analysis the association of weekly cisplatin was an independent significant predictive factor for OS (p=0.005) and DFS (p=0.017). More advanced age was an independent significant predictive factor for OS (p=0.005) and age > 80 years was a significant predictive factor for DFS (p= 0.026).

Conclusions: In general, advanced age is considered a negative prognostic factor, and less aggressive cares are

provided. Our results indicate that radiotherapy is a useful modality for elderly patients with cervical cancer, also for age over 80 years. The association of chemotherapy improves OS and DFS. The importance of radiotherapy will be greater in the aging society.

DP13

RADIATION THERAPY-DEPENDENT ORAL MUCOSITIS: HOW THE ORAL DYSBIOSIS MAY PREDISPOSE TO OPPORTUNISTIC FUNGAL INFECTIONS AND ORAL MUCOSITIS

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Aims: Oral mucositis (OM) is a common acute side effect of radiation therapy (RT) in head-neck cancer patients (HNCPs). Although clinical protocols advise the use of probiotics to counteract oral dysbiosis in OM, preclinical studies are needed to delineate the mechanisms by which the oral dysbiosis may predispose to OM. We performed an observational prospective study evaluating oral microbiota milieu during head and neck radiotherapy.

Method: We recruited HNCPs > 18 years old, undergoing RT alone or concomitant radio-chemotherapy (RT-CHT), +/- surgery. Non-naïve CHT patients who received antibiotic therapy in the two weeks prior to baseline were excluded. Acute toxicity was assessed using the CTCAE 5.0 grading. We monitored oral microbiome and lipidomics in correlation with RT-dependent OM at 0, 7, 15 days from the beginning of the RT-treatment and 1 month, 2 months post-RT treatment, using oral swab for metagenomics and lipidomics (OMNIgene ORAL kit). In addition, to understand the possible therapeutic effects of specific oral commensals we established an in vitro 3D tongue organoid model.

Results: Currently, 23 patients have been recruited. with an average age of 70 years. We performed a preliminary analysis on 17 patients who completed all scheduled tests. Median age was 70 years. Eight patients underwent RT at the primary site, and 9 at primary tumor site and neck lymphatic drainage. Median total RT dose to the primary tumor was 66 Gy (interquartile 62-66 Gy). Only 5 patients received cisplatin and 1 patient cetuximab. Most frequent acute RT-related side effects were: OM, dry mouth, dysphagia, fatigue; their appearance was related to the radiation dose. Metagenomics for 16S and 18S was performed for the first 4 patients (16S Bacteria and 18S Eukaryotes) and community diversity analysis was performed for the prokaryotic and eukaryotic population. Although preliminary, RT-related oral fungal infection was evident during therapy. The oral microbiome show for each patient a specific signature, although profound changes occur during RT. Regarding lipidomics, preliminary results show that the main lipid changes occur in the glicerophospholipid compartment. Organoid exposure to specific oral commensals restores the oral eubiome.

Conclusions: The present study represents an important tool to better delineate the oral myco/microbiome affected by RT±CHT, eventually leading to new mechanistic insights in advanced targeted therapy or OM prophylaxis protocols in HNCPs.

DP14

GENETIC PROFILE AND CARBON ION RADIOTHERAPY OF HEAD AND NECK ADENOID CYSTIC CARCINOMA: BALANCE NEEDLE FOR ONCOLOGICAL OUTCOME?

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Aims: To identify whether the presence of any mutation in Head and Neck Adenoid Cystic Carcinoma (HNACC) detected by Next Generation Sequencing (NGS) might affect oncological outcomes of a cohort of patients treated with definitive carbon ion radiotherapy (CIRT).

Methods: We performed a retrospective study on a cohort of twenty-eight patients with HNACC treated with definitive CIRT from March 2013 to March 2018 for whom NGS testing was available. Total CIRT dose was 68.8 Gy (RBE) in 16 fractions . Any mutations versus no mutation data confirmed by NGS were recorded to assess their impact on the outcome. Local control (LC) and overall survival (OS) were estimated according to Kaplan Meier curves. The associated Hazard Ratio (HR) was reported with the 95% confidence interval range (95% CI) and significance was calculated with the log-rank test.

Results: Overall, twenty-eight patients were included in this study. Fifteen patients (54%) had a silent NGS (group A), thirteen patients (46%) presented at least one mutation (group B): 5 patients had TP53 mutation (18%), 4 NOTCH1 (14%), 2 PIK3CA (7%), 1 PTPN11 (4%), 1 patient presented both APC and ATM (4%). After a median follow up of 57 months (range, 50-71 months), LC at 2 and 4 years was 40% and 30% for group A; 30% and 22% for group B (Figure 1). The OS rate for group A was 100% at 2-years and 94% at 4-years respectively. For Group B OS was 94% at 2-years and 68% at 4-years (Figure 2). The HR given by the presence of mutations at

NGS compared to no detection was for LC: 1,172 (range IC 95%: 0,472-2,908, p=0,73). The HR for OS was 2,954 (range IC 95%: 0,762-11,456, p= 0,11).

Conclusions: Based on our results, mutational status did not seem to influence outcomes of HNACC treated with CIRT. However, the possible selection bias of the cohort and the biological heterogeneity of the mutated patients may have influenced the results. Further studies are warranted to explore the role of the biology to predict the response to CIRT.

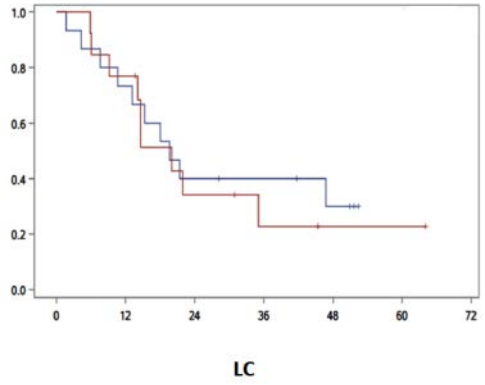

Figura 1 Kaplan Meier curve for LC: Group A- Blu; Group B - Red.

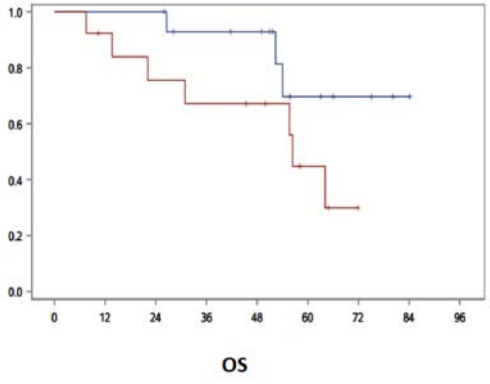

Figura 2. Kaplan Meier curve for OS: Group A-Blu; Group B - Red.

DP15

IMMUNE CHECKPOINT INHIBITORS AND CARBON ION RADIOTHERAPY (CIRT) IN SOLID CANCERS WITH STABLE DISEASE (ICONIC)

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Aims: Previous studies have described that radiotherapy (RT), in addition to immunotherapy, enhance the activity of immune checkpoint inhibitors (ICIs) increasing the immune response against tumoral cells. Recently, literature suggests that carbon ions (CI) may be more immunogenic than photons. So far, no clinical trials have been conducted to assess the safety of the association of ICIs and CIRT.We describe here the design of ICONIC, the first proof-of-concept of the feasibility and clinical activity of adding CIRT to ICI in oncology.

Methods:

Study Design: ICONIC is a multicenter, open label, non-randomized, phase II clinical trial aiming to assess the feasibility and clinical activity of adding CIRT to ICIs in advanced oligometastatic cancer patients with disease stability (SD) obtained with pembrolizumab administered as per standard of care. Twenty-seven patients with at least two measurable metastatic target lesions (at least one to be followed up as per RECIST and one suitable for CIRT) by Non-Small Cell Lung Cancer (NSCLC), Head and Neck Squamous Cell Carcinoma (HNSCC), melanoma or urothelial carcinoma will be eligible. High tumour burden (>10 lesions and/or a sum of diameters > 19 cm) will be considered as exclusion criteria. A safety run-in phase will be conducted throughout the study to monitor the toxicity.

Treatment: Patients under treatment with pembrolizumab monotherapy, administered within clinical practice, according to the Italian Drug Regulatory Agency

(Agenzia Italiana del Farmaco, AIFA), will be enrolled. After confirming SD, hypofractionated CIRT boost will be administered to one site of disease to a dose of 8 GyE/fr in 3 fractions. In case of multiple sites of metastases, the priority will be given to the symptomatic one followed by the potentially more immunogenic or feasible lesion.

Endpoints:The primary endpoint will be the effect of the combination; the secondary the safety profile and the impact on survival. Biological data of the enrolled patients will be collected for translational analysis.

Projected Results: in absence of published clinical trials, ICONIC will provide for the first time controlled data about the safety of the association of ICIs and CIRT.The results of ICONIC will represent a relevant contribution to the knowledge about the immunogenic alterations induced by CIRT,the feasibility and the clinical result of adding CIRT to ICIs in advanced metastatic tumors where immunotherapy is currently the standard of care.

DP16

ENHANCED RADIOSENSITIVITY IN HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC) MEDIATED BY GOLD NANOARCHITECTURES (NAS)

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Aims: Locally advanced HNSCC are characterized by high rate of recurrence resulting in poor survival. More effective therapies to improve the patient outcomes are a critical need. On this regard, noble metal nanoparticles (NPs) are emerging as promising agents in oncology as both drug carriers and radiosensitizers. On the other hand, co-treatments based on noble metal NPs are still at the preclinical stage because of the associated metal-persistence. Our group has recently developed the ultrasmall-in-nano architectures (NAs) which maintain the features of noble metal NPs avoiding the persistence issue. The aim of these study is to evaluate the *in vitro* efficacy of NAs as combined radiosensitizers.

Methods: We tested the effect of four different types of NAs on the ability of a single cell to grow into a colony after exposure to irradiation. The clonogenic assays was performed on two murine cell lines: the TC1/Luc (HPV positive model) and SCC7 (HPV negative model). Briefly, cells were plated in 6-well plates and then incubated for 2 h with the different NAs. After 24 h, the cells were X-irradiated (X-rad 320 kV, 15 mA) with doses from 2 to 8 Gy (TC1/Luc) and from 2 to 12 Gy (SCC7) and maintained for 7 days before staining with 1% crystal violet. Clonogenic survival curves were analyzed and radiosensitization enhancement ratio at 50% survival (ER50) was calculated.

Results: A significant radiosensitization was observed in both cell lines undergoing treatment with NAs, with ER50s ranging from 1.2 to 2,51. In both 2D models, we observed a synergistic effect of targeted-NAs compared with RT alone, whereas the other types of NAs show an additive effect with a reduction of clonogenic survival.

Conclusions: The addition of NAs to radiation induced a significant reduction of surviving fraction with a radiosensitizing effect in both cell lines. This effect is visible with all type of NAs and is more important for targeted-NAs. To enhance the potential translation to clinics of the nano-architectures, these data will be confirmed in advanced three-dimensional (3D) cancer models and *in vivo* using orthotopic models of head and neck cancer.

DP17

PHASE II NEVER TRIAL: PRELIMINARY EVALUATION OF THE SEGMENTATION QUALITY OF THE BENCHMARK CASE FOR RADIOMICS ANALYSIS

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Aims: The NEVER trial (Non-Elective Vulnerable Elderly Radiotherapy) is a single-arm, non-randomized, multicenter study that seeks to evaluate the outcome of a tailored radiotherapy (RT) approach in Head and Neck cancer (H&N) patients who are deemed unfit for standard curative treatments. The 15 participating centers were asked to perform delineation and planning of a benchmark case. The aim was to quantify the segmentation and dosimetric variability of the multicentric study in the perspective of radiomic analysis.

Methods: A two-steps revision was performed by four experienced radiation oncologists and three physicists: a quantitative and qualitative analysis was performed on the GTV-T and 5 OARs (glottic area, mandible, parotid glands, brainstem, spinal cord). The Dice Symilarity Coefficient (DS), Hausdorff distance and volume analysis were performed to compare each single center contours with the gold standard one. A dosimetric analysis was carried out to compare different treatment plans. A preliminary radiomic feature extraction was performed to identify a robust feature-set. All the data were extracted by using 3DSlicer® software dedicated tools.

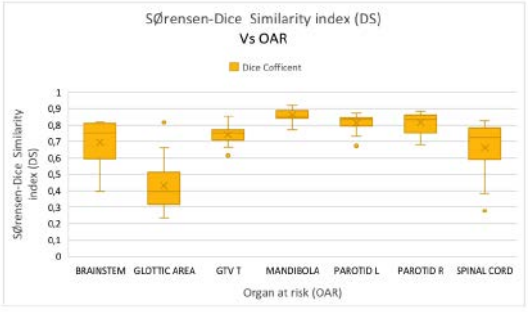

Figure 1. Sørensen-Dice Similarity index (DS) Vs OAR.

Results: A good performance in delineation of OAR was observed and showed by DSC in Figure 1, except for brainstem perhaps mirroring a lack of fusion CT-RT and MRI, spinal cord due to an extensive delineation of some centers, and glottic area. Remarkable results were obtained by DS, Hausdorff and volume analysis for GTV T: mean volume was of 11.11 cc ± 1.55 (mean± SD) that approaches to gold standard volume's (10.65cc). The analysis of achieved dosimetry plans evidenced that all values are close or below to the constraints values, except for glottic area and left parotid (omolateral to the GTV T). In total 120 different types of radiomic features (RFs) were extracted for each contoured structure and subdivided into the following classes: First Order Statistics (19 features), Shape-based (26 features), Gray Level Cooccurrence Matrix (24 features), Gray Level Run Length Matrix (16 features), Gray Level Size Zone Matrix (16 features), Neighbouring Gray Tone Difference Matrix (5 features), Gray Level Dependence Matrix (14 features).

Conclusions: The qualitative and quantitative analysis confirmed the good performance of different centers in processing the benchmark case. Further investigations have to be performed to understand the impact of inter-reader contouring variability on the extracted RFs.

DP18

RADIONECROSIS VERSUS PROGRESSION IN BRAIN TUMORS: RESULTS OF A PROMISING MRI TOOLS

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Introduction: Distinguishing between radiation necrosis (RN) and tumor progression in patients with irradiated primary or metastatic brain tumors, is a diagnostic challenge. Also, the use of new MRI sequences, like diffusion, perfusion-weighted, and spectroscopy, or PET with new amino acid tracers, is not always able to differentiate these two entities. To overcome this problem, encouraging results have been obtained from the analysis of delayed contrast extravasation MRI to calculate high-resolution maps, called "treatment response assessment maps" (TRAMs). This exploratory analysis aims to assess TRAM ability to differentiate between RN and tumor progression in a small cohort of brain tumor patients treated with radiotherapy (RT).

*Materials and Methods:*34 patients for 37 lesions irradiated were evaluated.14 patients were affected by primary brain tumors treated with surgery followed by RT and concomitant and/or adjuvant chemotherapy with temozolomide. 20 patients had brain metastases and underwent stereotactic radiosurgery (20-24Gy in 1fr), or hypofractionated stereotactic RT (27-30Gy in 3fr). All images were uploaded and elaborated into the image workstation ([Brainlab AG, Olof-Palme-Straße 9, 81829 Munich]). TRAMs were calculated by subtracting T1 MRI images acquired 5 minutes after contrast injection from the T1 MRI images acquired 60-105 minutes later. On TRAMs, radiation effects appeared as red areas whereas persistent tumoral lesions appeared as blue areas.

Results: From February 2021, 34 patients for 37 lesions irradiated have been evaluated, in a prospective study, with this MRI modality. During their follow-up, 13 patients (38%) showed a clinicoradiologic suspicion of persistent or progressive disease, and 21 (62%) a suspicion of RN. For 14 of them, a brain MET-PET has been performed. TRAMs analysis has shown a fair agreement with clinicoradiologic diagnosis, perfusion-weighted MRI, and

PET imaging, with an accuracy rate of the 81% in distinguishing radionecrosis and progression of disease versus 69% of the perfusion MRI. Furthermore, 11 of these patients underwent surgical resection, with histopathological confirm of persistent disease or radionecrosis.

Conclusions: These preliminary results show the ability of TRAMs in distinguish between RN and progressive disease. The recruitment of new patients continues, and further evaluations are ongoing to evaluate the sensitivity and positive predictive value of TRAMs analysis.

DP19

MENINGIOMA: THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO) SURVEY ON CURRENT MANAGEMENT

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Aims: Meningiomas are the most common primary intracranial tumors, of which most are classified as WHO Grade (G) I with a minority classified as WHO G II or G III. Neurosurgery is the first treatment option. Various radiotherapy (RT) approaches are often used to increase local control, especially if surgery alone seems insufficient. Meningiomas management is often defined on the basis of the Centre's experience. Therefore, the Central Nervous System Study Groups on behalf of the AIRO proposed a survey to investigated the current clinical practice in the Italian Radiotherapy Oncology Centres.

Methods: One dedicated radiation oncologist per Centre was asked to fill out the survey. Questions explored their attitude regarding G I, II and III meningiomas management: in which cases and how often the exclusive RT is proposed, which are the indications after neurosurgery, which technique and RT schedules are more used.

Results: The survey was filled out by 46 Radiotherapy Oncology Centres. The majority of responding Centres (72%) treated >50 brain tumors per year. In 80% of Centres there is a Neuro-Oncological board and 90% have familiarity with Stereotactic RT. About G I meningioma, the majority of responders do not propose adjuvant RT if neurosurgery is adequate. In patients with G II meningioma, 52% and 66% propose adjuvant RT after subtotal resection and in presence of unfavourable histological characteristics, respectively. Moreover, in patients with previous history of G II meningioma the attitude of many Centres is exclusive neurosurgery or neurosurgery plus adjuvant RT. In patients with G III meningiomas the majority propose adjuvant RT, regardless of surgery. In adjuvant setting, 81% of centres use IMRT with a total dose of 25 Gy in 5 or 27 Gy in 3 or 45 Gy in 15 fractions and 14-20 Gy in one fraction. Regarding salvage RT (tumor residual or relapse after neurosurgery) the most common fractionactions are 30 Gy in 3, 25 Gy in 5, 51 Gy in 17 fractions or 18-20 Gy in one fraction. In case of unresectable relapsing in-field meningioma, the majority have familiarity with reirradiation with moderated hypofractionaction.

Conclusions: Although there are wide variations in the prescription doses across the 46 Centres, the core indications for RT are reasonably consistent. These findings provide a basis for encouraging a national collaborative study to develop, implement, and monitor the use of RT in this clinical setting.

DP20

WHO IS THE REAL ELDER? OUTCOMES EVALUATION OF OVER 70-YEAR-OLD AND OVER 65-YEAR-OLD GLIOBLASTOMA PATIENTS WITH PROPENSITY SCORE MATCHED ANALYSIS

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Aims: The standard of care for elderly, newly-diagnosed glioblastoma (GBM) patients (pts) consists, if feasible, of surgical resection followed by a short course of radiation therapy (RT) with concomitant and adjuvant temozolomide (TMZ). To date, the literature lacks of consistence in the definition of elderly, if older than 65 years, or 70 years. Aim of this study was to explore whether differences exist between these two cohorts, comparing outcomes using a propensity score matched analysis (PSM).

Methods: 221 elderly newly diagnosed GBM patients were included and dichotomized in two groups: pts with 65–69 years of age and pts with ≥70 years. All pts received surgery followed by RT with concurrent and adjuvant TMZ. RT was performed within 4 weeks after surgery in both groups. The dose prescribed was 60Gy in 30 fractions for pts 65–69-year-old, or 40.5Gy in 15 fractions for ≥70-year-old. Corticosteroids were administered at low doses at the start of RT in both groups and progressively reduced during the course of RT in pts neurologically stable. In case of biopsy or gross residual tumor, steroids were given at higher doses. After 1:1 matching there were

86 pts in each group. Distribution of covariates was adequately balanced in the matched data set.

Results: After PSM, median progression-free survival (PFS) time and 1,2,3-year PFS rates were 10 months, 33.3%, 13.1%, and 6.6% for the 65–69-year group, 9 months, 34.7%, 11% and 4.8% for the ≥ 70-year group (p = 0.530). Median overall-survival (OS) time and 1,2,3-year OS rates were 14 months, 54.1%, 23.4%, 13.9% for the 65–69-year old group, 12 months, 49.3%, 21.5%, 10% for the ≥70-year group (p = 0.357). No differences were recorded in relation to different groups of age. RT has been interrupted in 11 (6.3%) cases: seven 65–69 years old pts receiving conventional RT schedule (60 Gy/30 fractions), and four ≥70 years old undergone hypofractionated RT regimen (40.5 Gy/15 fractions). After PSM analysis, the ECOG performance status (PS) and the extent of surgical resection have proven of impacting survival in 65–69-year group pts, while PS, MGMT status, and different adjuvant treatment performed, have proven of impacting survival in ≥70-year pts group.

Conclusions: The PSM analyses showed a similar outcome in 65–69-year old pts compared to older ones notwithstanding a more burdensome RT schedule. Hypofractionated RT treatment should be considered also in this group of younger elderly GBM pts.

DP21

KELOIDS POSTOPERATIVE RADIATION THERAPY: A SINGLE INSTITUTION EXPERIENCE

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Aims: Keloids are a benign fibroproliferative disease with high recurrence rate after surgical excision. Adjuvant radiotherapy is an option to reduce the risk of recurrence. The appropriate radiotherapy regimen for keloids is not yet clear. The aim is to present our experience in postoperative radiotherapy for recurrent keloids.

Methods: We retrospective analyzed outcomes of 6 patients (4 females, 2 males) treated in our Institute for a total of 8 keloids, from May 2021 to May 2022. All patients underwent one or more previous surgical treatments for recurrent keloids. Radiotherapy delivered with a 6-MeV electron beam started after 24 hours from keloid completely excision. A silicone bolus of 0.5-1 cm was applied on the keloid surgical scar to reach an adequate radiation dose to skin surface. For keloids located in the ear lobe, the day before surgery, we made a personalized high-density bolus (eXaSkin) to reduce dose to external auditory canal and mastoid bone (Figure 1A and 1D). Three-fraction schedule of 1950-2100 cGy (650-700 cGy/die) were used.

Results: The median age was 30 years (range 18-41), 2/6 patients were Caucasian. Four keloids were located in the ear lobe, 2 in the chest, 1 in the axilla and 1 in the shoulder. Factors contributing to keloid formation included piercing lesions (4/8); surgical scars (2/8 lesions) and 1 patient had a family history. Treatments were well tolerated without acute toxicity. The median follow up was 3 months, no recurrence and good cosmetic results were reported for all patients (Figure 1).

Conclusions: Radiotherapy treatment is a valid option to reduce keloids recurrence and improve cosmetic outcome but a multidisciplinary collaboration is necessary to achieve the optimal timing between surgery and radiotherapy. A longer follow-up is necessary to confirm these outcomes.

Figure 1.

DP22

WEEKLY HYPOFRACTIONATED RADIATION THERAPY FOR BASAL CELL SKIN CANCER FOR ELDERLY PATIENTS

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Aims: Basal cell carcinoma (BCC) of the skin is a very frequent malignancy that develops prevalently in people over 40 yrs. Surgery is actually the first choice for definitive treatment of localized BCC and only patients which refuse surgery or in which surgery is not indicated for age, comorbidities or tumor location are eligible to

radiotherapy. In order to improve the compliance of elderly patients to RT, with logistical and economic advantages, hypofractionation scheme could be considered. We reviewed cases of weekly hypofractionated RT in late elderly patiens.

Methods: patients (pts) with BCC were treated with definitive electron beam radiation with total dose of 24 Gy delivered in 3 weekly fractions. For all pts, photos were taken before RT starting and at 2 weeks, and-2 months after treatment's end, in order to independently assess clinical response. Acute and late toxicity were evaluated using the RTOG grading system. Cosmesis was defined according to Harris scale scoring system as "good", "fair" or "poor".

Results: During the last two years, 37 late elderly patients with high-risk localized BCC, were treated at our institution, with median age of 87 years (range: 73-101 years old). All BCC were located on the face or on the scalp; only 3 pts had BCC of the trunk. 23 BCC were < 2cm and 14 were between 2-5 cm. All patients completed the planned treatment. At the end of RT treatment 21 pts (56,8%) had complete response and 16 pts (43,2%) presented partial response. There were no differences in response rate when dividing the patients by the size of the lesions. About the patients who achieved complete response, none developed local recurrence at the last follow up control. The median follow up is 14 weeks, with 10 pts that haven't reached their follow up control after 8 weeks from the end of RT. Only 1 pt had G2 acute toxicity and no one had high-grade late toxicity. About the 10 pts who have not yet follow up control after 8 weeks, 4 (40%) had complete response and 6 (60%) presented partial tumor control rate. Cosmesis at the last control resulted "good" for 30 pts (81%) and "fair" for 7 pts (19%).

Discussion: Weekly hypofractionated RT is a good alternative to surgery for definitive treatment of localized BCC in late elderly pts with a good tumor control and good cosmetic outcomes. To evaluate the real effectiveness of this treatment, a follow-up of at least 8 weeks is necessary.

DP23

ELDERLY PATIENTS WITH NON MELANOMA SKIN CANCERS (NMSC) TREATED BY CONTACT HIGH DOSE RATE BRACHYTHERAPY(CHDR BRT)

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Aims: Non Melanoma skin cancers(NMSC) are the most common human malignancy in the world with increasing incidence in recent years. In this study we report the preliminary data concerning elderly patients with NMSC treated by contact Brachytherapy at High Dose Rate(cHDR BRT).

Patient and Method: All patients with NMSC enrolled in the study underwent cHDR BRT using applicators such as Freiburg Flap or silicone mould and I 192 source with remote afterloading.

Results: From May 2021 to June 2022, 8 patients, aged between 65 and 93 years (median age 88), were treated: 2 with primary BRT cHDR and 6 with post-operative BRT cHDR for a total of 12 lesions. The histological subtypes were: basal cell carcinoma and squamous cell carcinoma. The most common fractionation schemes used were the following: 45/40 Gy in 9/8 fractions. Two patients had acute G3 toxicity with resolution within two months. The patients are currently in the absence of local recurrence.

Conclusions: cHDR BRT is a safe and effective therapeutic option well tolerated for elderly patients with NMSC with good results in terms of toxicity and local control disease.

Table 1. Characteristic.

Age (years)	Median 88 (range = 65-93)
Gender	
Male	5
Female	3
Histology	
Basal cell carcinoma	3
Squamous cell carcinoma	5
Dose prescription	
40 Gy , 5 Gy /die , 2 days week	10 lesions
45 Gy, 5 Gy /die , 2 days week	2 lesions
Toxicity	
Grade 1	2
Grade 2	4
Grade 3	2
Grade 4	0

DP24

STEREOTACTIC ABLATIVE RADIOTHERAPY IN NEWLY DIAGNOSED AND OLIGO-METASTATIC LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS: SAFETY AND TREATMENT COMPLIANCE ANALYSIS OF THE START-NEW-ERA NON-RANDOMISED PHASE II TRIAL

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Purpose: To assess safety and treatment compliance of stereotactic ablative radiotherapy (SABR) in newly diagnosed unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients unfit for concurrent chemo-radiotherapy (ChT-RT) and oligo-metastatic (oligo-M) synchronous or oligo-progressive LA-NSCLC patients, enrolled in a single arm phase 2 study (Clinical trials.gov NCT05291780).

Methods and materials: Neoadjuvant ChT was prescribed in fit LA-NSCLC patients. The best systemic treatment according to driver mutations and PDL1 was prescribed in oligo-M NSCLC. The SABR tumor volume included primary tumor (T) and any regionally PET-CT positive node/s (N). To generate the planning target volumes (PTV) a margin of 5 mm was added to GTV-T and GTV-N, respectively.

Results: Between December 31, 2015 and December 31, 2021 64 LA-NSCLC and 24 oligo-M LA-NSCLC patients were enrolled. The median age was 73 years (range,39-89), 74 (84%) had ultra-central tumor. Thirty-five (55%) fit LA-NSCLC patients received neoadjuvant ChT, of these 10 sequential Durvalumab also; 15 (62%) and 3 (13%) oligo-M LA-NSCLC patients received Immunotherapy and TKI. Median prescribed dose was 45 Gy (range, 35-55) and 40 Gy (35-45) in 5 daily fractions to T and N, respectively. All patients completed SABR in a median time of 5 days (range, 5-7) and treatment compliance was 100%. Long-term clinical information about treatment safety was available for all patients. After a median follow-up of 23 months (range, 4-83) only one patient (submitted to ChT-SABR-Immunotherapy) developed ≥ grade (G) 3 esophageal toxicity.

Conclusions: In LA-NSCLC SABR was safe with a treatment compliance of 100%. Our outcomes would suggest the feasibility of using this approach in in newly diagnosed LA-NSCLC patients unfit for concurrent ChT-RT and oligo-M LA-NSCLC patients upfront or outback systemic treatment.

DP25

RADIOMIC-BASED STRATIFICATION OF HIGH-RISK PROSTATE CANCER PATIENT FOR THE PREDICTION OF BIOCHEMICAL FREE SURVIVAL

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Aims: The aim of the study is to investigate the prognostic value of CT-based radiomic features (RFs) for the prediction of biochemical free survival (BFS) in high-risk prostate cancer patients treated with radical radiotherapy (RT).

Method: Ninety high-risk prostate patients who were treated with RT between 2012 and 2019 were retrospectively included in the study. Radiomic features (RFs) were extracted from contrast-free treatment planning CT scans acquired using 120 kVp and 3 mm slice thickness on two CT scanners. Two volumes were segmented: prostate gland and seminal vesicles. Image analysis was performed with Pyradiomic library of 3D-Slicer. Before RF calculation CT images were resampled into isotropic voxels of 3mm. Up to 108 RFs were included for each volume. The pipeline included redundant RF elimination, RF standardization, feature selection (FS), RF categorization, univariate Cox regression and survival estimation by means of Kaplan Meier curves. Dataset was iteratively divided in training (T) – to select RFs and to estimate tuning parameters - and validation (V) – to make prediction only - using leave one group cross-validation (60% T-40% V, 1000 splits with endpoint balancing). During FS each RF was scored if its hazard radio (HR) p-value (P) in univariate Cox regression was < 0.05 before RF categorization (RFcat) and Log-Rank (LR) test P was < 0.05 after RFcat; top scored features were finally selected. RF median value on T was used as cutoff for RFcat to stratifying patients into high/low risk groups. The prognostic value of selected RFcat was assessed by the concordance index (CI). All results and P were expressed as mean values over 1000 T-V splits.

Results: Median follow-up was 47 (7–120) months; at 47 months BFS was 75.8% for the whole population. More scored RFs were GLSZM Small Area Emphasis (RFcat-1) and GLSZM Size Zone Non Uniformity (RFcat-2), both linked to seminal vesicles. LR P were 0.04 for both RFcat-1 and RFcat-2. HRs (95% conf.int) were 5.8 (1.3-28.5, P 0.05) and 4.2 (1.0-28.5, P 0.09) respectively for RFcat-1 and RFcat-2. CIs were 0.80 (T), 0.76 (V) for RFcat-1 and 0.82 (T), 0.8 (V) for RFcat-2.

Conclusions: Using a robust pipeline we found that RFs have a significant prognostic value for the prediction of BFS in high-risk prostate cancer patients. Features developments will be focused on the integration of our radiomic model to the clinical well-known predictor scheme and on the implementation of an external validation.

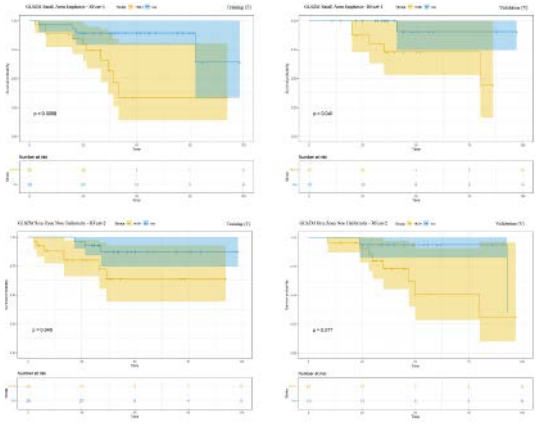

Figure 1.

DP26

HYPOFRACTIONATION IN BREAST CANCER: HAS THE COVID PANDEMIC CHANGED ITS USE IN LOMBARDY? - A SURVEY PROMOTED BY AIRO LOMBARDIA

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Aim: During the COVID pandemic, in Europe, hypofractionation was used more frequently, with the aim of reducing patients' (pts) hospital admissions. The aim of this work is to picture the use of hypo-fractionation for breast cancer in Lombardy and its implementation during COVID pandemic.

Methods: The regional executive committee of AIRO Lombardy proposed a survey, with multiple choice questions, concerning the use of ultra-hypofractionation (FAST forward trial), APBI, moderate hypo-fractionation and SIB and the implementation of such schedules in the course of the COVID pandemic. The questionnaire was sent by mail to the responsible for breast disease and to Director of each centre in May 2022.

Results: 2 centres did not respond as they do not treat breast disease; 27 of the remaining 33 centres filled the survey (81%). FAST-forward treatment (5,2Gy/26Gy) is performed in 56% of the centres, as normal clinical practice. Most centres choose it for >70y (53%), for Luminal A/B (80%), for NST cancer(93%) and early stage without macroscopic nodal involvement (Tis-T2, N0-N1mi) (80%). In 5 centres FAST schedule is performed also after adjuvant chemotherapy. 80% of centres foresee the use in case of negative or close margins (80%) and 67% select pts who can omit the sequential boost. 60% of the centres have implemented FAST to reduce the number of hospital access during a COVID pandemic. APBI is used as clinical practice in 67% of the centres; 3 of these increased the number of pts or implemented this schedule during COVID pandemic. In the same period, the number of pts treated with moderate hypofractionation increased in 26% of the centres. The irradiation of nodal stations, of skin, after mastectomy with/without breast implant and the concomitant chemotherapy are still factors that favour the choice of normofractionation. In 19 centres the SIB technique is used, especially with a moderate hypofractionation. SIB was also implemented during the COVID pandemic in 26% of Centres.

Conclusions: The COVID pandemic was one of the factors favouring the implementation of hypofractionated treatments, especially ultra-hypofractionated. It would be interesting to extend this survey on the national territory, with the aim of standardizing in the selection of pts. In some centres moderate hypofractionation remains unused in case of nodal or skin irradiation and after mastectomy.

Table 1. Descriptive analysis.

Type of Hospital	ASST	12	44%
	IRCCS	7	26%
	Private hospital	8	30%
University	University hospital	6	22%
	University affiliation	13	48%
	No university affiliation	8	30%
Ultra-hypofractionation in your Centre	Yes	15	56%
	no	12	44%
ULTRA HYPOFRACTIONATION (FAST FORWARD TRIAL) – sub analysis 15 Centres			
when do you use ultra hypofractionation?	As clinical practice	14	93%
	Only in clinical trial	1	7%
for which subtypes do you use this schedule?	Luminal A/B	12	80%
	Always (Luminal A/B, triple negative, Her2 positive)	1	7%
	Selected cases (>80y, logistic problem..)	2	13%
for which age groups do you use this schedule?	≥ 50 year	4	27%
	≥ 70 year	8	53%
	always irrespective of age	1	7%
	Selected cases (>80y, logistic problem..)	2	13%
You use this schedule if margins are:	Negative	8	53%
	Negative or close (< 2 mm)	4	27%
	Always (negative, close AND positive)	3	20%
with which fractionation do you deliver the boost?	Normo-fractionated boost	2	13%
	Hypo-fractionated boost (≥ 3 Gy/fr)	3	20%
	I only select the patients who, by risk class and age, can omit the boost	10	67%
Histology	All the hisotypes	9	60%
	Only NST	5	33%
	NST and lobular cancer	1	7%
Stage	Tis-T2 N0-N1mi	12	80%
	Tis-T2 N1a	3	20%
do you use this schedule after adjuvant chemotherapy?	No	10	67%
	yes	5	33%
what technique do you use? (multiple choice)	VMAT	10	67%
	IMRT	5	33%
	3D	10	67%
	Helical	2	13%
what kind of matching do you perform at LINAC?	Daily CBCT/MVCT	11	73%
	Daily EPID	3	20%
	EPID or CBCT only at first session	1	7%
during the COVID pandemic, have you implemented this schedule to reduce the number of hospital admissions?	yes, COVID was one of the factors in implementing this schedule	8	53%
	yes, COVID was the main factor in implementing this schedule	1	7%
	no, the pandemic did not influence the choice in the use of this schedule	6	40%
APBI			
do you use APBI in your centre?	No	9	33%
	yes	18	67%
when do you use APBI?	As clinical practice	17	94%
	Only in clinical trial	1	6%
during the COVID pandemic, have you implemented this schedule to reduce the number of hospital admissions?	yes, I did not use this schedule and this technique has been implemented	1	6%
	yes, I used this schedule but I increased the number of patients	2	11%
	no, the pandemic did not influence the choice in the use of this schedule	15	83%
MODERATE HYPO-FRACTIONATED RADIOTHERAPY			
during the COVID pandemic, have you implemented this schedule to reduce the number of hospital admissions?	yes, I increased the number of patients treated after mastectomy and needed nodal irradiation	4	15%
	yes, I increased the number of patients treated after conservative surgery	3	11%
	no, I treated the same number of patients	20	74%
When do you not use moderate hypo-fractionation? (multiple choice)	nodal irradiation	15	56%
	skin irradiation	12	44%
	unknown T	1	4%
	during adjuvant chemotherapy	7	26%
	after mastectomy	9	33%
	after mastectomy and positioning of implants	11	41%
	I use always hypofractionation	4	15%
SIB (simultaneous integrated boost)			
do you use SIB in your centre?	no	8	30%
	yes	19	70%
with which fractionation do you use SIB?			
	only with normofractionation	1	5%
	only with hypofractionantion	5	27%
	in both case	13	68%
When do you use SIB?	always, if boost is necessary	14	74%
	only if VMAT planning	4	21%
	only if electrons boost is not possible	1	5%
during the COVID pandemic, have you implemented this schedule to reduce the number of hospital admissions?	yes, I did not use this schedule and this technique has been implemented	3	16%
	yes, I used this schedule but I increased the number of patients	2	11%
	no, the pandemic did not influence the choice in the use of this schedule	14	74%

DP27

HYPOFRACTIONATION WITH SIMULTANEOUS INTEGRATED BOOST FOR EARLY BREAST CANCER PATIENTS: A LITERATURE REVIEW

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Aims: Moderate hypofractionation represents the standard of care for adjuvant whole-breast radiotherapy (WBRT). Several studies showed similar results in terms of local control and late toxicity as compared to conventional fractionation, optimizing patient and healthcare system resources. Scientific literature reports mostly the effectiveness and safety of hypofractionated sequential boost. Simultaneous integrated boost (SIB) may improve dose homogeneity, reducing overdosing in the breast outside the boost volume and has been introduced in combination with conventionally fractionated WBRT. Recently, several studies are investigating the feasibility of SIB in the hypofractionated regimen. We report a literature review of published studies evaluating SIB in hypofractionated schedule in order to assess the results in terms of clinical outcomes and early and late side effects.

Methods: A research on Medline (Pubmed) was performed using the following words: "*breast cancer radiotherapy*", "*simultaneous integrated boost*", "*hypofractionated radiotherapy*". Retrospective studies and review were excluded. Studies published since 2012 were included. Ten article, matching our criteria, were found. In each article, we collected the following data: number of patients, type of study, dose delivered to the breast and to the boost, radiotherapy technique, median follow-up, early and late toxicity, clinical outcomes.

Table 1. Characteristics, toxicities and clinical outcomes of 10 studies.

Study	Type of study	N° of patients	Dose whole breast (dose per fraction)	Dose boost (dose per fraction)	Technique	Follow-up	Acute toxicity	Late toxicity	Survival Outcomes
Scorsetti et al. (2012)	Phase I-II trial	50	40.5 Gy (2.7 Gy/fx)	7.5 Gy (0.5 Gy/fx)	VMAT	12 months (range=8–16 months)	G1=64%, G3=2%	0	----
Franco et al. (2013)	Prospective phase II trial	82	45 Gy (2.25 Gy/fx)	9 Gy (0.25 Gy/fx)	Tomotherapy	12 months (range=6–18 months)	G1=53%, G2=2%, G3=1%	G1=24%, G2=4%	LC=100%
Dellas et al. (2014)	Multicenter phase II study	151	40 Gy (2.5 Gy/fx)	7.5 Gy (0.5 Gy/fx)	3D-CRT or IMRT	----	G2= 22%(3D-CRT), 9% (IMRT)	----	----
Kyrgias et al. (2015)	Prospective study	77	46 Gy (2.3 Gy/fx)	8 (0.4 Gy/fx)	3D-CRT	24 months	G1=40.7%	G1=29.6%	----
Cante et al. (2015)	Observational study	83	45 Gy (2.25 Gy/fx)	5 Gy (0.25 Gy/fx)	3D-CRT	60 months (range=12-88 months)	G1=40%, G2=3%	G1=21%, G2=6%	5-year OS=92%, 5-year DFS= 100%
De Rose et al. (2016)	Phase I-II trial	144	40.5 Gy (2.7 Gy/fx)	7.5 Gy (0.5 Gy/fx)	VMAT	37 months (range 24–55 months)	G1=20%, G2=8%	G1=14%	----
Mondal et al. (2017)	Prospective study	10	40.5 Gy (2.7 Gy/fx)	7.5 Gy (0.5 Gy/fx)	VMAT	24 months (range=22-26 months)	G1=80%, G2=20%	----	----
Cante et al. (2017)	Observational study	178	45 Gy (2.25 Gy/fx)	5 Gy (0.25 Gy/fx)	3D-CRT	117 months (range=4-140 months)	----	----	10-year OS=92.2%, 10-year DFS= 95.5% 10-year LC=97.3%
Krug et al (2020)	Multicenter prospective single-arm phase II trial	143	40 Gy (2.5 Gy/fx)	7.5 Gy (0.5 Gy/fx)	3D-CRT or IMRT	----	----	G2- 14.7%	----
Franceschini et al (2021)	Phase I-II trial	450	40.5 Gy (2.7 Gy/fx)	7.5 Gy (0.5 Gy/fx)	VMAT	77 months (range=23-116 months)	----	G1=22%, G2=4% (6 months), G1=5.3%, G2=1.3% (5 years)	----

Results: The characteristics of the studies are summarized in Table 1. Upon studies, the median number of analyzed patients was 113 (range=10-450). All the analyzed studies were prospective. The most prescribed hypofractionated schedule consisted of dose to the whole breast of 40.5 Gy ranging from 40 to 46 Gy. The number of fractions varies from 15 to 20 fractions. The prescribed dose per fraction to the boost varied from 2.5 Gy per fraction to 3.2 Gy per fraction for a total boost dose ranging from 45 to 54 Gy. Clinical outcomes were reported as overall survival, disease free survival and local control in 3 of the examined studies with a longer follow up. Skin toxicity was described in all the studies, with low rate of early and late toxicity ≥G2.

Conclusions: Hypofractionated WBRT with Simultaneous Integrated Boost seems effective and well tolerate. Clinical randomized trial are needed to confirm these results.

DP28

SAFETY OF COMBINATION OF ABEMACICLIB AND RADIOTHERAPY IN METASTATIC BREST CANCER PATIENTS

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Aims: Little evidence regarding safety and efficacy of the combination of CDKIs plus radiotherapy (RT) is still currently available. Moreover the majority of studies report on the association of RT with Palbociclib or Ribociclib, less on Abemaciclib. The aim of this study is to evaluate the early toxicity of concurrent use of radiotherapy in association with Abemaciclib in patients with hormone-receptors positive metastatic breast cancer.

Methods: Records of patients with histologically proven metastatic or locally advanced breast cancer treated in our institution were reviewed. Patients who received radiotherapy and concurrent Abemaciclib were selected. Toxicity was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI-CTCAE V4.0).

Results: Eighteen consecutive metastatic breast cancer patients treated to 31 metastatic sites were studied. All patients (n=16, 100%) received Abemaciclib during radiotherapy course. 68% of patients received full dose of Abemaciclib during radiotherapy. The majority of treatments (77.5%) had a palliative intent (median dose= 30 Gy, range= 8-30 Gy). Four patients (22.2%) were treated to oligo-metastatic or oligo-progressive sites of disease with higher biological effective dose by stereotactic body radiotherapy (SBRT) (median dose = 30 Gy, range 21-30 Gy given in 3-5 fractions). Two patients (12.5%) were treated to chest wall skin disease (total dose 45 Gy). Two patients suspended RT and Abemaciclib due to haematological toxicity (one G3 neutropenia and one G3 anaemia). One patient treated to cervical spine experienced G2 esophagitis, one patient treated to chest wall develo-

ped G3 skin toxicity. Overall the rate of G3 toxicity was 16.6%. No patient presented diarrhoea during radiotherapy, even those treated to radiotherapy sites close to small and large bowel. Pain significantly improved after radiotherapy (mean value NRS pre-RT=3.9, SD=3.07; mean value NRS after RT=0.9, SD= 0.46; p=<0.0001)

Conclusion: Concomitant treatment of Abemaciclib and radiotherapy seems well tolerated showing acceptable toxicity.

DP29

FAST-FORWARD REGIME: OUR EXPERIENCE IN TERMS OF ACUTE AND EARLY-LATE SKIN TOXICITY

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Aims: The Fast-Forward (FF) trial showed that a five-fraction regimen of radiotherapy (RT) delivered in 1 week to the whole breast is non-inferior to the standard 3-week regimen. Based on the results of the FF trial, we opened a study with the same fractionated schedule regimen after the evaluation and approval by our Ethics Committee in patients with breast cancer in the early stage. We report acute and early-late skin toxicity.

Methods: From November 2020 to August 2021, 33 early BC patients (pts) received ultra-hypo fractionated whole breast irradiation (26 Gy in 5 fractions) after breast-conserving surgery with volumetric modulated arc therapy (VMAT) technique and daily IGRT. 7 pts (21%) underwent deep-inspiration breath-hold. According to molecular classification of St. Gallen Consensus 2011, all patients had luminal A. All pts were stratified by phototype according to the Fitzpatrick scale. The patient population includes invasive ductal or lobular carcinoma. The main exclusion criteria are carcinoma in situ, mastectomy and chemotherapy. Patients' details, and histological features are reported in the Table 1. Pts underwent follow-up clinical visits documented with photographs at the end of RT and 1, 6, and 12 months after RT-end to evaluate acute and subacute adverse effects. These are scored according to EORTC/RTOG and CTCAE (v.5) scales. Visits are integrated with an evaluation of redness skin in the photos through dedicated software.

Results: The median age is 73 years (range 65-86). Dose constraints to lung, heart and other organs at risk were respected in all pts. At the end of RT: 10 pts had G1 breast erythema. One month later, we found only 2 cases of self-resolved G1 breast fibrosis and 1 case of new-onset G1 breast hyperchromia, which persisted for three months. Three months later, we found benign mastitis. One year later, a keloid in the chirurgical area.

Conclusions: Our data confirmed the tolerability and safety of the FF regime in terms of very low acute and early-late skin toxicities, despite elderly pts with fair skin phototypes.

Table 1.

Patients' characteristics	Number of patients (%)
T stage	
T1a	9 pts (27%)
T1b	13 pts (39%)
T1c	11 pts (34%)
Grading	
G1	17 pts (51%)
G2	16 pts (49%)
Fizpatrick scale	
Phototype 1	7 pts (21%)
Phototype 2	19 pts (57%)
Phototype 3	5 pts (15%)
Phototype 4	2 pts (7%)
Phototype 5	0 pts (0%)
Phototype 6	0 pts (0%)

DP30

ONE WEEK PARTIAL BREAST IRRADIATION: SURVIVAL AND TOXICITY ANALYSES OF 134 PATIENTS

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Aims: Partial Breast Irradiation (PBI), according to ASTRO and ESTRO guidelines, is a valid option for very early-stage Breast Cancer (BC) patients. Nevertheless, there is still lack of consensus about the best treatment schedule to use. In this study, we aimed to collect data from BC patients who underwent PBI in one week.

Method: We retrospectively analyzed survival and toxicity data of BC female patients treated in our institution from 2014 to 2022. Inclusion criteria were age > 45, breast conservative surgery for BC of any histology or grading, T=1, N=0/mic. Gross Tumor Volume (GTV) was defined as the breast tissue between surgical clips;

Clinical Target Volume (CTV) was an isometric expansion of 1.5 cm from the GTV, cropped into the breast; Planned Target Volume (PTV) was CTV + 0.5mm of isometric expansion. The treatment schedule was 30 Gy delivered with VMAT in 5 daily fractions, prescribed at the 95% of the dose to the PTV.

Results: One hundred thirty-four patients with a median age of 68 (46 – 83) years were included in the study. Half (67/134) of the cases were left breast; 124/134 (93%) were ductal invasive carcinomas, 3/134 (2%) were lobular invasive carcinomas, and 7 (6%) were other histologies; 133/134 (99.3%) were Grading (G) 1 or 2 and 1/134 (0.7%) were G3. Median dimension of the lesions was 8 mm (1 – 19); 108/134 (80%) and 26/134 (20%) were Luminal A and B, respectively. Two patients had close positive (<1 mm) margins. No patients interrupted therapy, with a median overall treatment time of 5 (5 – 8) days. No ≥ G3 acute nor late toxicities were reported. There were 2/134 (1.4%) cases of G2 acute fibrosis, and 2/134 (1.4%) patients experienced G2 late toxicities: one asthenia and one fibrosis. Three (2%) patients reported late cardiac major events, but all of them were treated on the right breast. No pulmonary late toxicities were detected. Good or Excellent cosmetic evaluation sec. Harvard Scale were assessed in 112/134 (83%) cases by the physician VS 108/134 (80%) cases by the patients. After a median follow-up of 32 (6 – 95) months, 132/134 (98%) patients were alive and 3/134 (2%) experienced local recurrence [1/3 (33%) was homolateral]. Three years Disease-Free Survival and Overall Survival were 98% (95% C.I. 77% – 99%) and 98% (95% C.I. 90% – 99%) respectively.

Conclusions: Accordingly with our previous results on acute toxicity, "One week - PBI" proves to be a safe and effective treatment that can be offered to early-stage BC Patients.

DP31

AXILLARY LYMPH NODES INCIDENTAL DOSE WITH STANDARD 3D-CRT: A RETROSPECTIVE STUDY

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Aims: In the past, axillary dissection (ALND) represented the preferred treatment in patients with clinically negative axilla and positive sentinel lymph node biopsy (SLNB), completing tumour staging and providing local control (LC). ACOSOG Z0011, comparing patients treated with or without ALND in cN0 and SLNB+, showed ALND safely omission, leading to focus on incidental dose to the axilla eradicating additional unseen axillary lymph nodes metastases. Nevertheless, the correlation between the adequate coverage of the the incidental dose to the axilla, remains debated. We aim to evaluate the incidental axillary dose in pN+ patients treated with only breast radiotherapy.

Methods: We retrospectively analyzed breast cancer patients treated in our Center. All patients received breast conservative surgery (BCS) without ALND and were treated with breast conventional fractionated 3D-CRT without intentional axillary irradiation. A retrospective delineation of axillary level I (L1) and axillary level II (L2) was performed according to ESTRO contouring guidelines. A dosimetric evaluation was conducted. Clinical outcomes as overall survival (OS), disease-free survival (DFS) and LC were analysed.

Results: Fifty-two patients undergone to BCS and SLNB with pN1 were analyzed. Median age was 58 years (range=38-73 years). Dosimetric values were reported in Table 1. The mean breast PTV volume was 776.8 cc (range=218.1-1287,9 cc) with a median maximal dose of 5328 cGy (range= 5258-5428 cGy) and a median mean dose of 5000 cGy (5000-5073 cGy). The mean L1 and L2 volumes were 59.31 cc (range=15.2-127.8 cc) and 10.9 cc (range=4.4-60.2 cc) respectively. For L1, the median maximal and mean doses were 4921.5 cGy (range= 495-5334 cGy) and 1791 cGy (1659-4143 cGy) respectively. For L2, the median maximal and mean doses were 4649 cGy (range= 46.35-5022 cGy) and 1021 cGy (range= 20.29-2972 cGy), respectively. No patient had complete coverage of L1 and L2 as demonstrated by the median $V_{47.5}$ and V_{45} coverage. The median follow up was 52.7 months (13.8-87.4 months). The 4-year OS, DFS and LC were 100%, 88.5% and 94.2% respectively; one patient presented axillary relapse.

Conclusion: In this study, incidental dose to axillary levels with 3D-CRT, did not delivered a therapeutic dose to L1 and L2. When required, definitive irradiation of the L1 and L2 needs a modification of standard tangential fields and the targeting of axillary lymph node volumes, in addition to the breast gland volume.

Table 1. Incidental dose evaluation on Axillary Levels I and II.

	Volume cc (range)	D_{max} cGy(range)	D_{mean} cGy(range)	$V_{47.5}$		V_{45}		V_{40}		V_{5}	
				cc (range)	% (range)	cc (range)	% (range)	cc (range)	% (range)	cc (range)	% (range)
Level I	58.97 (15.2-127.8)	4921.5 (495-5334)	1791.0 (1659-4143)	1.7 (0-27.3)	2.9 (0-21.3)	8.14 (0-37.6)	13.8 (0-29.4)	18.4 (0-49.4)	31.3 (0-38.7)	37.9 (7.9-79.7)	64.4 (51.7-2.3)
Level II	9.7 (4.4-60.2)	4649.0 (46.35-5022)	1021.5 (20.29-2972)	0 (0-2.0)	0 (0-3.3)	0.2 (0-13.1)	2 (0-21.8)	1.3 (0-30.2)	13.5 (0-50.1)	4.1 (1.2-53.0)	41.6 (26.4-8.0)

DP32

IMMUNE RESPONSE EVALUATION IN OLIGORECURRENT AND OLIGOPROGRESSIVE PROSTATE CANCER PATIENTS TREATED WITH METASTASES-DIRECTED STEREOTACTIC BODY RADIATION THERAPY (SBRT) WITH AND WITHOUT CONCOMITANT ANDROGEN DEPRIVATION THERAPY: PRELIMINARY RESULTS OF I.OSCAR STUDY

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Aims: Metastatic dissemination is the major cause of mortality in patients affected by advanced prostate cancer (PCa). Stereotactic body radiation therapy (SBRT) showed strong clinical benefits in the treatment of oligometastatic PCa. Moreover, SBRT seems to increase the immunosuppressive subsets including tumor-associated macrophages (TAMs) and regulatory T cells (Treg cells) in the tumor bed, and to modulate immune dynamics in the peripheral blood of cancer patients. However, the impact of SBRT on the immune composition of patients affected by PCa still needs to be determined.

Material and Method: We profiled the immune composition of fresh blood of 20 patients affected by 33 oligometastatic PCa lesions before and after administration of SBRT on the metastatic site. Treatment was delivered with (55%) or without (45%) concomitant androgen deprivation therapy, and prescription doses ranged from 30 to 45 Gy in 3 to 6 fractions, with a median EQD2 of 54.69 Gy. The primary endpoint was the identification of SBRT-driven immune changes.

Results: We performed multiparametric flow cytometry (FACS) analysis on fresh peripheral blood collected before SBRT administration (T0), just after the last fraction (T1) and 7 days after the treatment (T2). We investigated the phenotype, functional state and modulations of CD8+ and CD4+ T lymphocytes, CD4+ T regulatory cells, Natural Killer cells (NK) and myeloid subsets (monocytes, Dendritic cells (DCs), neutrophils and eosinophils). Longitudinal analysis of lymphoid populations revealed a significant increase of Treg cell abundance over time (percentage of Treg on CD45+, T0= 0.19% ± 0.21 vs T2= 0.32% ± 0.19, p= 0.048, paired t test) and an increase in total NKs (percentage of NK on CD45+, T0= 2.52% ± 2.44 vs T2= 5.5% ± 4.41, p= 0.049, paired t test). The number of CD8+ and conventional CD4+ was not affected by SBRT delivery, but we observed a decrease in T effector memory subsets that was reflected by an enrichment in naive populations. No significant changes in frequency and activation were detected on myeloid subsets.

Conclusions: Our early results provides a comprehensive analysis of the peripheral immune landscape in PCa patients exposed to metastasis-directed SBRT. Immune profiling identified modulations in the immune dynamics following SBRT administration. Our results may lead to the identification of immune alterations that can be exploited to develop novel combinatorial strategies.

DP33

SAFETY AND CLINICAL OUTCOME OF 1.5T MR-GUIDED STEREOTACTIC BODY RADIOTHERAPY (MRGSBRT) TO LYMPHNODE OLIGOMETASTASES FROM PROSTATE ADENOCARCINOMA

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Aim: stereotactic body radiotherapy (SBRT) has been commonly used for several years in the treatment of prostate adenocarcinoma (PCa) lymphnode oligometastases. In the present prospective observational study are reported the safety and outcome of PCa lymphnode oligometastases treated on 1.5T MR-Linac.

Material and Methods: PCa lymphnode oligometastases treated with daily adapted MR-guided SBRT using homogeneous dose range (35-40 Gy in 5 fractions) were included in the analysis. 117 nodal oligometastases from PCa in 62 patients were treated on 1.5T MR-Linac. The primary end-point was the local control. Additionally, toxicity and pattern of progression were evaluated.

Results: Median treatment duration was 24 minutes (range 21-30). Adaptive workflow consisted of: adapt to shape in 87% fractions and adapt to position in 13% treatment sessions. Median PSA before SBRT was 0.82 ng/ml (range 0.22-7.37). Pretreatment PET was: PSMA in 82% of cases and choline in 18%. Median PET SUV was 8.6. The margin between GTV and PTV was 3 mm in 79 cases and 5 mm in 38 cases. In 21 patients (34%) MRgSBRT was associated with concomitant hormone therapy. The median follow-up was 12 months (range 3-24 months). The 12-months local control (LC) was 93.3%, the median progression-free survival (PFS) was 10.3 months (range 8.5-19.9), whereas the median nodal progression-free survival (NPFS) was 19.9 months (range 10.3-22.3). All patients are still alive. Globally 46 patients nodally progressed as follows: 35 (76%) in a different nodal station, 7 (15%) in the same nodal station, and 4 (9%) in a combination of same and different nodal station. At multivariate analysis, a statistically significant correlation both between median PET SUV >8.6 and NPFS, and between hormone therapy administration pre-SBRT and NPFS was found (p=0.0). Neither PSA value pre-SBRT seems

impact on NPFS nor margin GTV-PTV seems impact on local progression free survival (LPFS). Toxicity was assessed by means CTCAE v.5 and was characterized by 4 (6%) cases of grade 1 fatigue and 2 (3%) grade 1 diarrhea.

Conclusion: SBRT on 1.5T MR-Linac guarantee high local control levels on PCa lymphnode metastases. Toxicity is minimal. Future studies will explore the role of dose escalation to further increase local control and the reduction of treatment margins.

DP34

SINGLE TREATMENT PLANNING FOR ROBOTIC RADIOSURGERY/STEREOTACTIC RADIOTHERAPY FOR MULTIPLE BRAIN METASTASIS

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Background: Stereotactic radiosurgery (SRS)/fractionated stereotactic radiotherapy (SRT) prescription was extended to patients with multiple (≥5) brain metastases. Here we report our experience with single treatment planning SRS/SRT delivered with CyberKnife® (Accuray, Sunnyvale, CA) in pts with ≥5 brain metastases.

Material and Methods: From 03/2018-03/2022 a total of 677 brain metastases in 58 pts were treated with a single treatment plan SRS (23 pts) or SRT (11 pts with 3 fractions and 24 pts with 5 fractions) in our institution. Patient's median age was 61 (27-84) years. Primary tumor was lung in 29 pts, breast in 14 pts, melanoma in 7 pts, gynecological cancer in 2 pts, kidney in 2 pts, parotids in one patient, 2 patients had lung and breast cancer, and one patient had lung and prostate cancer. Eight pts were previously treated with Whole Brain Radiotherapy (WBRT). Gross target volume (GTV) and organs at risk (OAR) were defined on a contrast-enhanced T1-weighted MRI fused to simulation computed tomography (CT). A 1 mm margin was added to GTV to define Planning target volume (PTV).

Results: Median number of brain metastases was 8 (5-45). Median GTV 1.78 (0.41-28.82) cc, and median PTV 5.38 (1.31-37.8) cc. Median prescribed dose was 30 (22-37.5) Gy, at the 78 (65-89) % median isodose, in a median of 3 (1-5) fractions, delivered in consecutive days. With a median follow of 6.6 (0.5-23.3) months 29 pts were dead. Acute toxicity was as follows: 3 pts presented G1 dizziness, 2 pts G1 headache, 2 pts G1 nausea, 2 pts G1 hemiparesis (weakness), and 1 patient G1 vomiting. No patient presented radionecrosis. Overall Survival (OS) at 6-, 12- and 18-months was 64.1%, 50%, and 35.3, respectively. Six-, 12- and 18- month Local Relapse Free Survival (LRFS) was 87.2%, 72.5% and 72.5% (see Figure 1), and Intracranial Relapse Free Survival (IRFS) 61.5%, 46.2% and 40.4%, respectively.

Conclusion: SRS/SRT in pts with ≥5brain metastases is feasible with a good toxicity profile and it is a promising option of treatment in these pts.

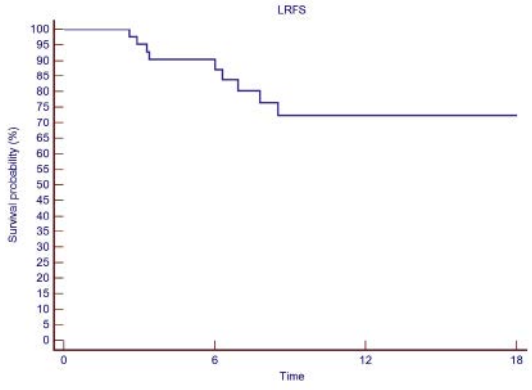

Figure 1.

DP35

LATTICE RADIATION THERAPY FOR BULKY CACERS: A CASE SERIES

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Aims: The management of bulky cancer represents a concerning issue since surgery is often excluded, systemic therapies have poor efficacy, and standard radiotherapy achieves limited response. Lattice radiation therapy (LRT) is an innovative technique based on the inhomogeneous target irradiation, according to the so-called Lattice framework. This is an array where ablative dose areas (namely, vertices or hotspots) are separated by lower dose regions called valleys, with a valleys-vertices dose escalation of at least 250% of the valleys prescibed dose. The aim of this study is to explore the toxicity and the response of large tumors management with LRT.

Methods: From October 2021, 6 palliative patients with bulky unresectable cancers have been treated with LTR, namely: 2 lung cancers, 2 melanomas, 2 ovaric cancers. Median patients' age was 71.5 years (range 68-85 years). The prescription dose was 20-30 Gy to the entire lesion volume with a simultaneous dose escalation up to 55-66.7 Gy on the vertices, delivered in five daily fractions over one week; no support therapy was required and

daily IGRT-VMAT was performed for all treatments.

Results: Before LTR, all patients were symptomatic due to the bulky tumors (ECOG 2-3). The median tumor volume was 927 cc (range 223 – 3274 cc). Half of the patients experimented a G2 astenia (CTCAE v5.0) post-LRT while the other half reported a G1. One lung patient had a G2 esophagitis while one ovaric patient reported a G1 cystitis and proctitis. No acute toxicity > G2 was observed. At 3 months follow up CT, 3 patients and 2 patients presented partial response (PR) and stable disease (SD) respectively, according to RECIST1.1 criteria, while 1 patient died due to lung metastasis progression, despite irradiated lesion PR. All patients reported a symptoms relief with an improvement of their daily activities (ECOG 0-1). At 6 months re-assessment 1 patient died due to a bacterial pneumonia, 1 patient reported a limited disease progression while 4 patients maintained the SD response. Despite a general slight asthenia (G0/G1), all patients were in good general condition (ECOG) 0-1, and no other toxicity.

Conclusions: Albeit the little number of patients, the short follow up and the different bulky cancer types, these are the first LRT treatments done in our Center and provide further data on LRT planning. In our case series, LRT appears to be associated with an interesting large lesions response without an increase in toxicity.

DP36

MRI BEFORE SALVAGE RADIOTHERAPY AFTER RADICAL PROSTATECTOMY FOR PROSTATE CANCER: A MULTICENTRE CASE-CONTROL STUDY

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Aims: Current international guidelines recommend choline-PET or PSMA-PET in patients with prostate cancer candidates for salvage radiotherapy (RT) to rule out the presence of lymph node or hematogenous metastases prior to RT. However, in our centers, we tested the use of pelvic MRI in order to evaluate its effectiveness in detecting locoregional relapses and therefore to optimize salvage RT. Therefore, the aim of this analysis is to compare two matched cohorts of patients who underwent or did not undergo MRI before salvage RT in terms of biochemical disease control.

Method: One hundred sixteen patients from three centres were included in this study. Patients in the two cohorts were matched according to: PSA before SRT (<0.2; 0.2-0.5; 0.5-1.0; >1.0 ng/ml), pathological tumor stage, ISUP grade group (1, 2, 3, 4, 5), pelvic nodal irradiation, and adjuvant hormonal therapy. Kaplan-Meier survival curves were compared using the log-rank test. This analysis is part of a multicenter observational study (ICAROS trial) approved by the ethics committees of the participating centers.

Results: Macroscopic locoregional relapse was identified in forty-two/58 patients (72.4%) undergoing pelvic MRI and therefore these patients were treated with a median total dose of 70.4 Gy (range: 66-72.6), while patients without MRI or with negative MRI received a median total dose of 66 Gy (range: 62.5-72.0). Indeed, in patients with MRI-detected relapse, a focal boost (sequential or concomitant) was administered with a median dose of 4.4 Gy (range: 4.4-70.5). Overall, comparing the cohorts of patients who underwent and did not undergo MRI, a significantly higher rate of biochemical relapse-free survival was recorded in the first group (2-year rates: 91.5% *versus* 73.6%; p = 0.006; Figure 1).

Conclusions: An unexpectedly and surprisingly high rate of macroscopic relapses was recorded in patients undergoing MRI prior to salvage RT. This made it possible to adapt the treatment by delivering a boost to the disease site. This strategy produced a significant improvement in the biochemical outcome of these patients. Our findings challenge current guidelines on the pre-treatment restaging in this setting.

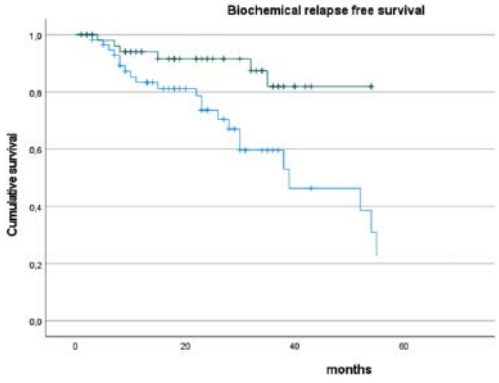

Figure 1. Biochemical relapse-free survival in patient undergoing MRI (green) and not undergoing MRI (blue) before salvage radiotherapy (p<0.001).

DP37

ADJUVANT RADIOTHERAPY OF PROSTATE CANCER: A MULTICENTER COMPREHENSIVE ANALYSIS OF ACUTE AND LATE TOXICITY PREDICTORS

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Aims: Aim of this study was to analyze the prognostic impact on toxicity, in patients with prostate cancer treated with adjuvant radiotherapy, of several patients and treatment characteristics.

Method: Both acute and late toxicity were assessed in this observational study (ICAROS-1). The recorded and evaluated patients-related characteristics were age and Charlson's comorbidity index. Analyzed treatment characteristics were: delivery of prophylactic lymph nodes irradiation, previous TURP, use of adjuvant ADT and its type (LH-RH analogues or high-dose Bicalutamide) and duration, RT fractionation and technique (including type of image-guidance systems), and Equivalent Dose in 2 Gy/fraction (EQD2) to the prostate bed and pelvic lymph nodes. Late toxicity-free survival curves were calculated by the Kaplan-Meier product-limit method and compared with the log-rank test. Variables with p value less than 0.05 or with a trend ($p < 0.1$) at univariate analysis were entered into a multivariate Cox's regression model. Acute toxicity was assessed by RTOG scale while late toxicity was evaluated with the RTOG/EORTC scale.

Results: Three-hundred-eighty-one patients were enrolled. Acute GI and GU G3 toxicity rates were 0.5% and 1.3%, respectively. Median EQD2 to the prostate bed ($\alpha/\beta=1.5$) was 71.4 Gy. Most patients (75.4%) were treated with IMRT/VMAT techniques. No patient showed G>3 acute toxicity. At multivariable logistic regression only younger age (< 65 years) was significantly correlated with increased acute toxicity (both GI and GU). Five-year GI and GU grade ≥ 3 late toxicity-free survival was 98.1% and 94.5%, respectively. The only significant correlation at Cox's regression model was in terms of reduced risk of GI toxicity in patients undergoing hypofractionation (HR: 0.38; 95%CI: 0.18-0.78; p: 0.008).

Conclusions: "Modern" postoperative radiotherapy is safe, both in terms of acute and late effects, also in subjects undergoing hypofractionated regimens and especially in elderly patients.

DP38

ABSTRACT NOT PUBLISHABLE

DP39

NUTRITIONAL AND INFLAMMATORY STATUS AS PREDICTIVE BIOMARKERS IN OLIGORECURRENT PCA (RADIOSA TRIAL)

M. Zaffaroni[1], G. Marvaso[1,2], G. Corrao[1], M.G. Vincini[1], M. Pepa[1], A. Gaeta[1], S. Gandini[1], D. Zerini[1], F. Mosè Castronovo[1], F. Cattani[1], F.A. Mistretta[1], S. Luzzago[1], G. Musi[1,2], S. Alessi[1], C. Fodor[1], G. Petralia[1], G. Pravettoni[1,2], O. De Cobelli[1,2], R. Orecchia[1], B.A. Jereczek-Fossa[1,2]

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Aims: Stereotactic body radiotherapy (SBRT) is emerging as a low-toxicity treatment for prostate cancer (PCa), allowing to postpone androgen deprivation therapy (ADT) in the oligometastatic setting. In phase II randomized clinical trial RADIOSA the biology task comprises the identification of predictive and prognostic biomarkers in oligorecurrent-castration-sensitive PCa setting in order to discriminate poly- from oligo-metastatic patients who could really benefit from metastases-directed-therapies.

Methods: Patients were stratified into two treatment groups according to ADT administration and site of metastases. Common serum-derived biomarkers were collected at baseline, 3, and 6 months after RT. Controlling nutritional status (CONUT) score, used to assess patient nutritional status, and prognostic nutritional index (PNI), an immunity and nutrition-based prognostic score, were calculated according to available literature. Neutrophil-lymphocyte ratio (NLR) and NLR-albumine ratio (NLRAR) were evaluated as inflammatory status scores. Significant differences were evaluated by stratifying patients for ADT administration (arm B *vs* A, yes vs no) and site of metastases (bone vs lymph node) with non-parametric Wilcoxon rank-sum test.

Results: Sixty-two patients were included in the present analysis (33 arm A, 29 arm B). When patients were stratified by ADT administration (Figure1a), cholesterol values showed an increasing trend in group B ($p < .001$), and the change in albumin level was also different between the 2 groups ($p = .01$). When patients were stratified by site of metastases (Figure1b), the values of NLR and NLRAR were found to be increased in patients with bone localizations ($p=.01$ and $p=.03$, respectively).

Conclusion: Cholesterol and albumin changes appear

to be affected by ADT addition, a well-known factor for quality-of-life worsening. Moreover, inflammatory status seems to be related to site of metastatic localization as bone lesions, known as slightly worse in terms of response than lymph node-only sites, resulted associated with a higher inflammatory status. Analysed parameters appear as interesting candidates to be possibly included in clinical decision-making in order to stratify patients who would benefit from more or less aggressive treatments. Further evaluations and correlations with clinical outcomes and longer follow-up are needed for the validation of these candidate biomarkers.

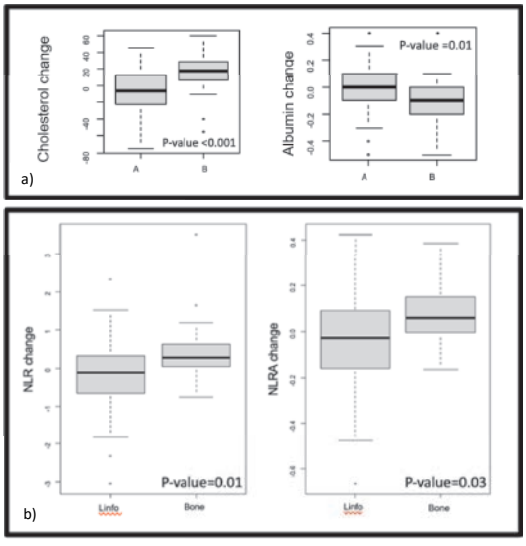

Figure 1. Cholesterol and albumin change in the cohort of patients stratified by treatment arm (a) and NLR and NLRAR change in the cohort of patients stratified according to the site of metastases (b).

DP40

CYBERKNIFE ULTRA-HYPOFRACTIONATED SBRT FOR LOCALIZED PROSTATE CANCER WITH DOSE-ESCALATION TO THE DOMINANT INTRA-PROSTATIC LESION: IN-SILICO PLANNING STUDY

G.C. Mazzola[1,2], G. Marvaso[1,2], G. Corrao[1], D. Zerini[1], S. Durante[1], A. Vavassori[1], M.G. Vincini[1], M. Zaffaroni[1], E. Rondi[1], S. Vigorito[1], F. Cattani[1], B.A. Jereczek-Fossa[1,2]

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Aims: Based on the results from the PACE-B trial reporting a toxicity advantage for CyberKnife linacs vs SBRT ones, the aim of the present study is to compare dose distribution plans between ultra-hypofractionated (UH) IMRT with Vero™ system (BrainLAB) and UH SBRT with CyberKnife™ system (Accuray Inc) using image-guided virtual fiducial markers tracking, for localized prostate cancer (PCa) with simultaneous integrated boost (SIB) to the dominant intraprostatic lesion (DIL).

Method: Five of ten planned patients with at least one DIL visible on multi-parametric magnetic resonance imaging (mpMRI) scan were analysed for an in-silico planning study comparison. Median dosimetric parameters were compared between patient-delivered Vero™ IMRT and virtually-delivered CyberKnife™ SBRT plans with 95% isodose prescription level to the planning target volume (PTV), aiming to perform UH schedule for both explored techniques of 40 Gy in 5 fractions (8 Gy/fx) to the DIL (PTV-DIL) while treating the whole prostate gland (PTV-P) to 36.25 Gy in 5 fractions (7.25 Gy/fx) every other day, using a 5mm isotropic margin, except 3mm posteriorly, for PTV-P and 3 mm isotropic margin for PTV-DIL.

Table 1. Median dose parameters across all patients for IMRT Vero™ and SBRT CyberKnife™ plans. List of abbreviations: IMRT (intensity modulated radiotherapy); PTV-DIL (Planning target volume – dominant intraprostatic lesion); PTV-P (Planning target volume – prostate gland); SBRT (stereotactic body radiotherapy).

		IMRT Vero™	SBRT CyberKnife™
PTV-DIL (40 Gy)			
D 0.03cc	(%)	103.80	105.10
V110%	(%)	0.00	0.00
D98%	(%)	97.80	97.99
D95%	(%)	98.20	98.37
D2%	(%)	103.77	104.84
D50%	(%)	101.10	100.62
P-PTV (3.25 Gy)			
D 0.03cc	(%)	110.50	115.97
D98%	(%)	94.00	91.34
V110%	(%)	0.40	0.00
D95%	(%)	96.10	93.87
D50%	(%)	100.10	101.35
D2%	(%)	106.60	109.64
Rectum			
V18 Gy	(%)	14.88	25.30
V29 Gy	(%)	3.73	5.50
V33 Gy	(%)	1.00	1.30
V36 Gy	(%)	0.20	0.10
Anal canal			
Dmean	(Gy)	10.70	12.07
Bladder			
V36 Gy	(%)	0.92	0.60
V36 Gy	(cc)	3.80	2.51
V18 Gy	(%)	23.60	30.00
Bowel			
V30 Gy	(cc)	0.00	0.00
V17Gy	(cc)	0.00	0.46
Penile bulb			
V29 Gy	(%)	0.00	0.00
Penis			
V13 Gy	(cc)	0.30	0.82
Testis			
D20%	(Gy)	0.14	0.33

Results: Both SBRT CyberKnife™ and IMRT Vero™ plans can produce clinically acceptable SIB plans to a dose of 40 Gy in 5 fractions but comparison of the coverage of PTV volumes established that small difference exists (Table 1). In comparison with the SBRT

CyberKnife™ plans, IMRT Vero™ technique allowed slightly superior dose coverage for PTV-P (D95% = 93.87% vs 96.10%) while nearly the same coverage was achieved for DIL PTV (D95% = 98.20% vs 98.37%). Regarding the organs at risk (OARs), both techniques were able to maintain the dose distribution well below the dose constraints. Overall, the IMRT Vero™ technique got the best results in sparing the rectum and bladder volumes, while substantially no difference was observed for anal canal, penis, testis, penile bulb and bowel bag volumes. Except for one patient was not possible for SBRT CyberKnife™ technique to respect one of the three bladder constraints (V36Gy<5cc = 6.48cc).

Conclusions: This preliminary in silico planning comparison showed that UH CyberKnife™ SBRT with SIB for localized PCa appears to be feasible but data needs to be confirmed with the analyses of the other five patients planned in this study. Different SBRT CyberKnife™ plans isodose prescription levels at 85% and 65% will be performed for final in-silico comparison.

DP41

PREDICTIVE FACTORS OF LATE GENITOURINARY TOXICITY AFTER CYBERKNIFE RE-IRRADIATION FOR LOCALLY RECURRENT PROSTATE CANCER

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Aims: Management of prostate cancer local relapse after postoperative or definitive radiotherapy (RT) include re-irradiation with stereotactic body RT (re-SBRT). However, dosimetric predictive models are needed to improve treatment planning in this scenario. The aim of our study was to develop a model predicting genitourinary (GU) toxicity in patients (pts) undergoing re-SBRT with Cyberknife® robotic system for locally recurrent prostate cancer.

Method: Data from 90 pts treated at our institution from June 2012 to June 2021 were collected. All pts had undergone definitive or postoperative radiotherapy and were affected by biochemical relapse (as defined by European Urology Association Criteria). Intra-prostatic or prostate bed recurrence was detected by 18F-choline PET/CT and MRI; pts with metastatic or regional nodal disease were excluded. All pts were treated with CyberKnife® robotic system, for a total dose of 30 Gy in 5 fractions. Toxicity was recorded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Logistic regression analysis was used to test the relationship between late GU toxicity and Gross Target Volume cubic centimetres (ccGTV), Dose to 50% of urinary bladder volume (DB50), Maximum dose within Planning Target Volume (Dmax), urethra Dmax (UDmax) and Total Equivalent Dose (tEQD2) administered to prostate or prostate bed.

Results: After a median follow up of 48.1 months (range 3.6-104.1), late GU toxicity occurred in 29 pts (32%). A predictive model for late genitourinary toxicity was developed using the logistic regression model. Overall, the model fitted the data with a significance level of p=0.01. There was no significant impact of ccGTV (p=0.84), DB50 (p=0.09), Dmax (p=0.07), and tEQD2 total (p=0.9) with late GU toxicity; only UDmax exhibited a significant association (p=0.01). A receive operating characteristic (ROC) curve was used to look for the optimal cut-off point for UDmax, that is predictive for late GU adverse events (Figure 1). ROC analysis showed that UDmax >32.2 Gy best predicted GU toxicity, with a positive likelihood ratio of 1.3 (95% CI 1.1-1.5) (AUC 0.6, p=0.06).

Conclusions: These data suggest that higher doses to the urethra may increase the risk of late GU toxicity. After a 4-year follow-up, given the low number of events, re-SBRT proved to be safe in locally recurrent prostate cancer pts. However, more data are warranted to define a predictive model that allows the most accurate patient selection.

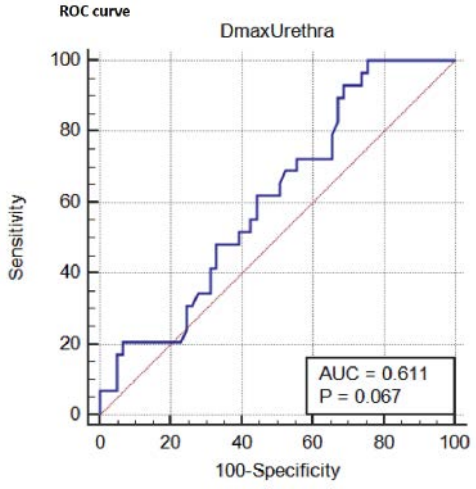

Figure 1. ROC curve for Dmax Urethra (UDmax). A UDmax >32.2 Gy is best predictive of GU toxicity, with a positive likelihood ratio of 1.3 (95% CI 1.1-1.5) (AUC 0.6, p=0.06).

DP42

PRELIMINARY REPORT OF TOXICITY AND QUALITY OF LIFE OF THE FIRST 100 PATIENTS TREATED WITH 1.5T MR-GUIDED STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER

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Aims: In the present series we report preliminary acute and late toxicity, and quality of life assessment of the first 100 patients who received 1.5T MR-guided daily-adaptive stereotactic body radiotherapy for prostate cancer.

Methods: We report the outcomes of the first 100 patients treated from October 2019 to December 2020, enrolled in a prospective study. The insertion of the rectal spacer was proposed as optional and applied in 37 patients. Hormone therapy was prescribed in 32 patients. Toxicity and quality of life were prospectively assessed.

Results: 100 patients with median age 71 years (range, 52-84) were treated with 1.5T MR-guided daily adaptive SBRT in 5 sessions for a median total dose of 35 Gy (35-36.25 Gy) on consecutive (n=75) or alternate days (n=25). Acute toxicity rates were as follows: 5 acute G2 genitourinary tract pain events, 4 cases of G2 events. With a median follow-up of 12 months (3-20), for late events, we have recorded 3 late G2 GU events and one G3 GU event for a patient who received a TURP 8 months after radiotherapy. For late GI events, we have recorded 3 G≥2 GI proctitis, including one argon laser treatment for radiation-induced proctitis. All patients are alive and in disease control except for one M1-low volume patient who developed distant progression two months after RT. Preliminary QoL assessment revealed a global trend towards resolution within the second follow-up, except for sexual functioning. Interestingly, global health perception resulted improved after one year of follow-up compared to baseline scores.

Conclusions: 1.5T MR-guided daily-adaptive SBRT for prostate cancer reports excellent results in terms of toxicity and minimal impact on QoL. More mature data are warranted.

DP43

CASTRATION RESISTANCE AND PREVIOUS SALVAGE THERAPY IMPACT ON OUTCOMES OF LYMPH-NODAL METASTATIC PROSTATE CANCER PATIENTS TREATED WITH SALVAGE ENRT AND PET GUIDED SIB

A. Fodor[1], C.L. Deantoni[1], L. Giannini[1], S.L. Villa[1], P. Mangili[2], M. Midulla[1], I. Dell'Oca[1], F. Zerbetto[1], L. Perna[2], S. Broggi[2], R. Tummineri[1], A. Del Vecchio[2], C. Cozzarini[1], C. Fiorino[2], N.G. Di Muzio[1,3]

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Aims: Choline and PSMA PET/CT have anticipated the diagnosis of prostate cancer (PCa) lymph-nodal metastases (LNM). Generally, patient population is heterogeneous including either hormono-sensitive (HSPC) or castration-resistant patients (CRPC), at the first or second relapse (already treated with adjuvant or salvage radiotherapy, ART/SRT), who could have different prognoses. Here we report long-term outcomes of our cohort of patients treated with salvage extensive–nodal radiotherapy (ENRT) considering these differences.

Methods: From 02/2005 to 04/2021, 192 PCa patients were treated for LNM with ENRT at a median total dose (TD)= 51.8 Gy/28 fr, and Choline PET/CT guided simultaneous integrated boost (SIB) on PET+ LN to a median TD= 65.5 Gy. One hundred seventy-nine patients were previously treated with surgery, and 114 of them with ART/SRT. Median age at relapse was 70.0 (50.2-87.4) years. Median PSA was 2.09 (0.18-187.0) ng/ml. Median number of PET+ LNM was 2 (1-20). Androgen Deprivation Therapy was prescribed for 100 patients, for a median of 25 months, not prescribed for 41, and 51 were CRPC.

Table 1. Biochemical Relapse-Free Survival (bRFS); Disease-Free Survival (DFS) and Overall Survival (OS) in hormonosensitive versus castration resistant prostate cancer patient and in patients with first versus second relapse after surgery.

bRFS years	HSPC vs CRPC (192 patients)			First relapse vs second relapse after surgery (179 operated on patients)		
	HSPC (%)	CRPC (%)	p	1°relapse (%)	2°relapse (%)	p
2	71.8	28.8		78,9	48,2	
3	63.1	17.7	<0.0001	71.2	37.9	<0.0001
5	45.7	8		54.1	23.8	
DFS years						
2	91.9	73.9		95.9	82.2	
3	84.5	69.1	0.03	92.8	72.2	0.03
5	75.3	59		84.9	63.9	
OS years						
2	92.1	88.2		94.5	87.6	
3	87.4	66.2	<0.0001	84	79.8	0.02
5	76.9	50		77	66.1	

Results: Median follow up was 62 (4.1-171.2)

months. Median PSA after the treatment was 0.05 (0.0-5.05) ng/ml, then 64.6 % of patients presented a biochemical relapse, 30.2% a clinical relapse (only 4.7% in the field of SRT), and 43.2% were dead (22.4% from prostate cancer). Two-, three- and five-year Kaplan Meyer estimates of biochemical relapse-free (bRFS), disease-free (DFS) and overall survival (OS) in HSPC vs CRPC and in the 179 operated on patients with first LNM relapse (without previous RT) vs second LNM relapse (with previous ART/SRT) are presented in Table 1.

Conclusions: In our large cohort of patients treated with ENRT and Choline PET/CT guided SIB for LNM, with a long follow-up, CRPC patients (who were generally not at the first relapse) and patients with second relapse after surgery already treated with ART/SRT have a statistically significant worse evolution than patients still HSPC, or at the first relapse after surgery.

DP44

EXTREME HYPOFRACTIONATED LINAC-BASED STEREOTACTIC RADIOTHERAPY FOR PROSTATE CANCER PATIENTS: PRELIMINARY ANALYSIS OF A PHASE II TRIAL

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[1]Radiation Oncology Department, General Regional Hospital F. Miulli; [2]Urology Department, General Regional Hospital F. Miulli, Italy

Aims: Stereotactic body radiation therapy (SBRT) with extreme hypofractionation is replacing prostatectomy mostly in case of low-risk prostate cancer (PC). However, in selected case of intermediate/high risk, it could be a treatment justified solution. Aim of this study is to evaluate safety and efficacy of Linac-based SBRT in patients affected by PC.

Method: Men affected by localized PC were enrolled and analyzed. The SBRT schedule consisted of 35 Gy in 5 fractions administered with Volumetric arc therapy in 1 or 2 weeks based on target volume and urinary symptom. According to risk group androgen deprivation therapy (ADT) was prescribed in some cases. Toxicity was assessed at the end of treatment, 2 weeks after SBRT and during follow-up (fu) using the Common Terminology Criteria for Adverse Events. PSA values were recorded before treatment and during fu as biochemical response criteria.

Results: Between July 2019-September 2021, 156 patients were treated. Median age was 75 years (range 50-86); 42% were low-risk, 42% favorable/unfavorable intermediate-risk and 16% high-risk group. Median pretreatment PSA was 6.36 ng/ml (range 0.2-49.5 ng/ml). ADT was administrated in 65 patients. Median PTV was 101.7 cc (range 51-192.2). Median baseline IPSS was 6 (range 0-19). At the end of treatment, no >G1 acute toxicity was observed. At 2-3 weeks after treatment, 7 patients reported G2 acute genitourinary toxicity (urinary frequency, urinary tract pain and urinary retention), while 21 patients referred rectal tenesmus. During the last fu, no late toxicity and no relevant deteriorations of QoL were described. At a median fu of 23 months (range 8-35), excellent biochemical disease control was achieved in all cases with median PSA of 0.5 ng/ml (range 0-7.21).

Conclusions: Linac-based SBRT in patients affected by localized PC is feasible and well tolerated with excellent biochemical disease control.

DP45

STEREOTACTIC BODY RADIOTHERAPY WITH CYBERKNIFE® SYSTEM FOR LOW-AND INTERMEDIATE-RISK PROSTATE CANCER. CLINICAL OUTCOMES AND TOXICITIES OF CYPRO TRIAL

V. Borzillo[1], R. Di Franco[1], E. Scipilliti[1], F. Savino[1], S. Falivene[1], F. Cammarota[1], M. Serra[1], S. Mercogliano[1], A. Crispo[2], S. Pignata[3], S. Rossetti[3], G. Quarto[3], P. Muto[1]

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Aims: Stereotactic body radiotherapy (SBRT) is an emerging treatment approach for Low-and Intermediate-Risk (LR-IR) Prostate Cancer (PC). We present the clinical outcomes and toxicities of the CyPro Trial.

Methods: 122 low and intermediate-risk PC patients were treated with Cyberknife System (CK) at dose of 35 or 36.25 Gy in five fractions. Biochemical failures (BF)/ biochemical disease-free survival (bDFS) was defined using the Phoenix method (nadir + 2 ng/mL). Rectal and urinary acute/late toxicity was scored on the Radiation Therapy Oncology Group (RTOG) toxicity scale, quality of life (QOL) was assessed with EORTC QLQ C30 and PR25. International Index of Erectile Function-5 (IIEF5) and International Prostatic Symptoms Score (IPSS) questionnaires administered.

Results: The median follow-up was 4 years (range, 3-60 months). At 84 months bDFS was 96.2% for LR and 94.2% for IR (Figure 1). In all patients, we recorded a median nadir PSA value of 0.13 ng/mL and earlier its achievement and more significant reduction in the PSA value in the group treated with the highest dose. Urinary toxicity >G2 was: acute G3 0% and G4 1%; late G4 1%. acute and late rectal toxicity >G2 was 0%. There were no significant differences in toxicity or quality of life between the two dose groups. For erectile dysfunction, we found differences based on the patients age but not on

the dose.

Conclusion: CK SBRT is a valid therapeutic option in the treatment of patients with LR-IR PC with good biochemical control and QOL. We found no differences in biochemical control and toxicities in relation to dose.

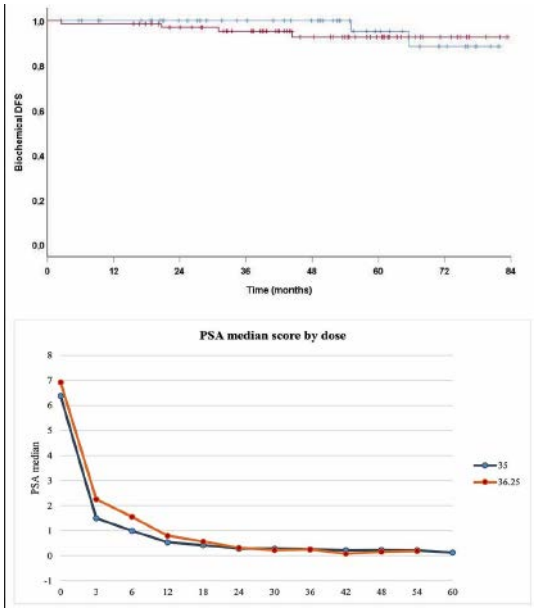

Figure 1.

DP46

ACUTE END CHRONIC GASTROINTESTINAL TOXICITY OF HIGH RISK PROSTATE CANCER PATIENTS TREATED WITH WHOLE-PELVIC RADIOTHERAPY: CORRELATION WITH PERITONEAL SPACE DOSE

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Aims: Pelvic irradiation for high-risk prostate cancer seems to improve biochemical-failure-free survival, disease-free survival and overall survival but it is limited by gastrointestinal (GI) toxicity. Small bowel injury has been described by the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) with a threshold dose of grade 3 or greater toxicity when 195 cc of the contoured peritoneal space receives ≥45Gy while Landoni et al. proposed different constraints suggesting V15Gy <1100 cc, V45Gy <250 cc, V30Gy <500 cc and 10-20% of the total volume. The aim of our analysis was to evaluate the correlation of peritoneal space dose with GI toxicity in high-risk prostate cancer patients treated with whole-pelvic radiotherapy.

Method: Thirty-two (32) patients with high-risk prostate cancer were enrolled in this analysis and all patients were treated with a total dose of 50-54 Gy (1.8-2 Gy per fraction) to the whole-pelvis with intensity-modulated and VMAT technique. The following dosimetric constraints were applied to the peritoneal space: V15 <1100 cc, V30 <500 cc, V30 between 10-20%, V45Gy <195 cc and <250 cc. GI toxicities were graded using RTOG grading. The dose-volume histograms for peritoneal space were calculated by the independent t-test and analysis of GI toxicity was performed with the independent t-test or Chi-square/Fisher exact test.

Results: PTV coverage was reached for all treatment plans. Median follow-up was 26 months. No G3-G4 acute or late toxicities were observed. Fifty percent (50%) of patients experienced acute and/or late G1-G2 toxicities. Median V15 was 320 cc for patients without toxicity and 980 cc for patients with G1-G2 toxicity ($p<0.001$), median V30 was 270 cc and 14% for patients without toxicity and 568 cc and 48% for patients with G1-G2 toxicity ($p<0.001$). Median V45 was 60 cc for patients without toxicity and 180 cc for patients with G1-G2 toxicity ($p<0.001$).

Conclusions: Our analysis shows that the volumes of irradiated peritoneal space in patients who experienced grade 1-2 gastrointestinal toxicity were significantly larger than those in patients who experienced grade 0 gastrointestinal toxicity and this was valid for both acute and chronic. Particularly V30Gy seems to be related to GI toxicity, even in patients with a respected V45Gy. Low-dose peritoneal irradiation plays a role in GI toxicity, considering that V15Gy is significantly higher in patients with bowel injury. Dose to the peritoneal space should be minimized in order to improve quality of life of patients treated with pelvic radiotherapy for prostate cancer.

DP47

ADDED VALUE OF MRI RADIOMICS TO PREDICT PATHOLOGICAL STATUS OF PROSTATE CANCER PATIENTS

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Aims: Unlike radical prostatectomy, radiotherapy lacks a definitive pathological assessment of performance, and consequently patients can be under- or overtreated. The purpose of this study was to evaluate the ability of radiomic features to improve the accuracy of non-invasive prediction of pathological features of prostate cancer with prostatectomy as confirmation.

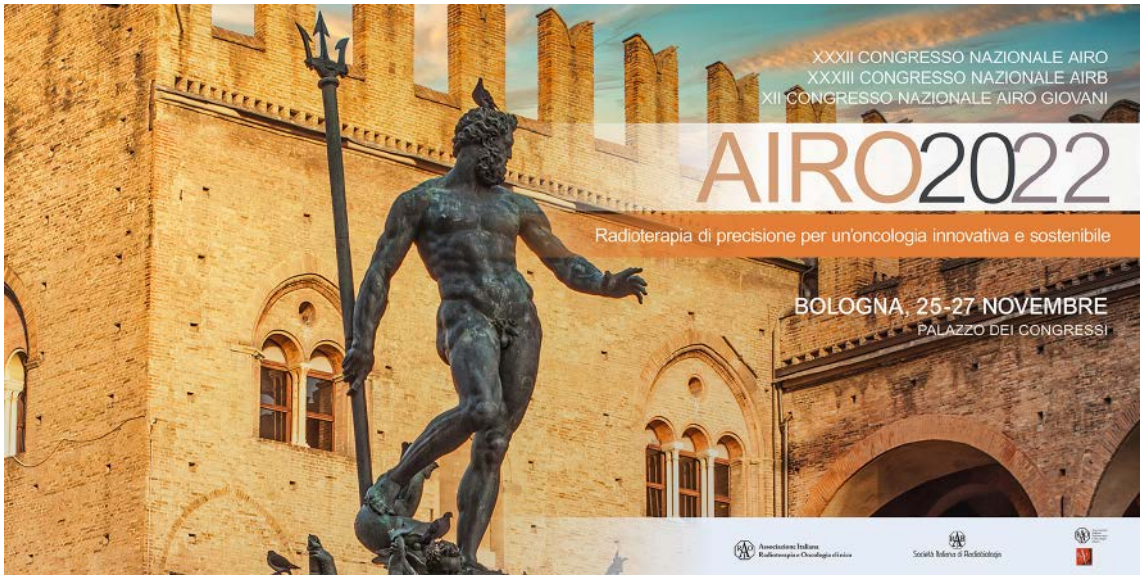
Methods: A representative subset of 100 patients from a cohort of roughly 1500 who have undergone multiparametric magnetic resonance imaging (mpMRI) of the prostate and prostatectomy in our Institution since 2015 was selected. The prostate of each patient was segmented from T2-weighted MR images by an expert radiologist, and used in the extraction of 1810 radiomic features (PyRadiomics 3.0.1, AIM Harvard), successively reduced to 50. Gradient-boosted decision tree models were separately trained using clinical features (age, prostate volume, iPSA, PI-RADS category, biopsy-based total Gleason score, ISUP grade, and risk class) alone and in combination with the radiomic features to predict surgical marginal status (R0 vs R1), the presence of pathological lymph nodes (pN0 vs pN1), pathological tumor stage (pT2 vs pT3), and ISUP grade group (<3 vs ≥4) and validated with 32-times repeated 5-fold cross validation. The models were evaluated and compared in terms of their AUC values.

Results: The addition of radiomics features led to increases of AUC ranging between 0.061 (pT) and 0.139 (ISUP grade group) as summarized in Table 1. All AUC gains were statistically significant at a level of at least 0.0001 (Mann-Whitney U-test).

Conclusions: Our results highlight the potential benefit of whole-prostate radiomics for prediction of all the examined pathological features of prostate cancer, with AUC values in the 0.80-88 range. Literature models have used baseline clinical and mpMRI-based variables to predict cancer aggressiveness. The potential of a radiomic plus clinical feature model to better predict pathological features of prostate cancer, and in particular extraprostatic extension and pelvic lymph node involvement, is of considerable interest for guiding the clinical decision-making process and can provide valuable information for personalizing therapy. These preliminary but promising results will be validated in the larger cohort of 1500 patients.

Table. 1 AUC values and 95% confidence intervals over repeated validation folds of the trained models*. *all differences between clinical and radiomic models significant at p<0.0001 (Mann-Whitney U-test).

	Surgical marginal status	Pathological lymph nodes	Pathological tumor stage	ISUP grade group
Clinical	0.715 (±0.008)	0.797 (±0.012)	0.733 (±0.005)	0.739 (±0.010)
Radiomic	0.800 (±0.007)	0.871 (±0.010)	0.795 (±0.006)	0.877 (±0.009)



Poster

P001

IMMUNOLOGICAL PROFILE AND CYTOKINE DYNAMICS IN HEAD AND NECK CANCER PATIENTS TREATED WITH RADIO-IMMUNOTHERAPY

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Aims: We conducted a translational study on enrolled patients in a phase I/II trial of anti PD-L1 durvalumab (Du) combined with cetuximab (Ctx) and radiotherapy (RT) in locally advanced squamous cell carcinoma of the head and neck. The aim was to evaluate the immunological profile and to investigate the dynamics of cytokine production in peripheral blood mononuclear cells (PBMCs).

Methods: Nine patients were enrolled. Blood samples were obtained at 3 different time points: T0 at the moment of the recruitment, T1 two weeks after the beginning of the RT and Du-Ctx therapy, and T2 three months after the last RT session, during immunotherapy. PBMCs were isolated to perform flow cytometry and ELISA analysis. Flow cytometry data analysis was performed with Flowlogic 7.3. The expression of phenotypic markers on circulating T cells and NK cells was evaluated by the percentage of positive cells. PBMCs were cultured with and without T cell stimulation anti-CD3 for 24h. Then, the cytokine concentration for IL6, TGFβ, IL10, IFNγ and galectin1 in PBMC culture supernatants were measured in a quantitative sandwich ELISA. Statistical analysis was performed using GraphPad Prism 6.01. One-way analysis of variance (ANOVA) was performed.

Results: We analysed the immunophenotype of circulating total T cells (CD3+) and total NK cells (CD56+ and/or CD16+). Our results showed in all the patients a similar proportions of circulating T cells and NK cells, with a mean of 53.50% of T cells and 2.63% of NK. Flow cytometry analysis showed among T cells a higher percentage of CD4+ cells (65,57% ±12,54) compared to CD8+(23,31 ±13,60) ($p<0.05$) and among NK cells a higher percentage of CD16+ cells compared to CD56+ and CD56dim ($p<0.05$). The relative capacity of PMBCs for cytokine production *in vitro* was next addressed and cytokine dynamics evaluated. We observed a significant decrease of IL6, IFNγ and galactin1 at T1 compared to T0. Production was restored at T2 and at T1 after T cell activation with anti-CD3. Production of IL10 significantly decreased at T2 and it was not restored with anti-CD3. TGFβ production didn't show significant change at the evaluated time points.

Conclusions: Flow cytometry analysis showed that CD4/CD8 ratio was in the range of European general population. CD16+ NK were more represented in enrolled patient compared to health population. The dynamics of cytokine production suggests an immunomodulatory effect of combined treatment RT + Du + Ctx.

P002

RADIOMICS ANALYSIS OF MESORECTUM IN RECTAL CANCER TO PREDICT SURVIVAL OUTCOMES

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Aims: The standard treatment for locally advanced rectal cancer (LARC) is neoadjuvant chemoradiation (nCRT) followed by total mesorectal excision (TME). Several studies have shown that radiomics can predict patologic complete response (pCR) and survival outcomes. Mesorectal fat might contain important prognostic information in patients with LARC (tumoral deposits, lymph node involvement). Therefore, the aim of this study was to investigate the correlation between mesorectal radiomics features with pCR and 2-years Disease Free Survival (2y-DFS)

Methods: LARC patients with a diagnostic pre- and post- nCRT Magnetic Resonance Image (MRI) treated at a single institution from May 2008 to November 2016 with a follow-up of at least 5 years were retrospectively enrolled and analyzed. All patients underwent surgery. The dataset was firstly randomly split into training set validation set (66%/34%, Tripod 2a). MRI radiomic features before and after nCRT were extracted from GTV and mesorectum, which were blindly contoured by two radiation oncologists expert in rectal cancer. The radiomic characteristics of the mesorectum and GTV, and clinical variables were selected for model development. The performance of the pCR and 2y-DFS predictive models was evaluated in terms of area under receiver operating characteristic (ROC) curve (AUC) for both training and validation set.

Results: Overall 203 LARC patients were collected (71 female, 132 male; median age 65 years; median dose delivered to the GTV 55Gy; median follow-up 95 months). Overall pCR was 26.6% and overall 2y-DFS was 84.3%. A total of 565 variables (273 mesorectal features, 273 GTV features, 19 clinical variables) were extracted. 91 Radiomic features were extracted from MRI pre and post CRT. Delta radiomic features were calculated as the ratio between features extracted at the two time points. The best-performing pCR predictive model was based on GTV_ERI (Early Regression Index) and mesorectal features with an AUC of 0.80. The best-performing 2yDFS predictive model was based on two features (Delta L-least GTV and Energy Pre-Mesorectum) with an AUC of 0.76 and 0.70 in the training and validation set, respectively.

Conclusions: The results of this study suggest a possible role of mesorectal radiomics features in predicting pCR and 2y-DFS for LARC patients. Further analyses is needed to better understand the role of specific mesorectal features in predicting survival outcomes in LARC.

P003

MRI-DERIVED RADIOMICS ON MICROENVIRONMENT TISSUE HETEROGENEITY TO GUIDE POST-OPERATIVE MANAGEMENT OF GLIOBLASTOMA: TOWARD PERSONALIZED RADIATION TREATMENT VOLUME

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Aims: The use of medical imaging, as a non-invasive tool to derive prognostic factors, is becoming increasingly popular. Given its propensity to spread to areas of brain parenchyma surrounding the surgical cavity, a generous margin is typically included in the clinical target volume (CTV) and some strategies have been explored to spare the surrounding normal tissue. Radiomics is the put extraction of quantitative features from radiographic images. The GLIFA project (GLIoblastoma Feature Analysis) is a multicentric project planned to investigated the role of radiomic analysis in GBM management, to verify if radiomic features in the tissue around the resection cavity which may guide the radiation target volume delineation.

Methods: We retrospectively analyzed radiomic features extracted from 90 patients with total or subtotal resection, who completed the standard adjuvant treatment. The Manual segmentation was performed on post gadolinium T1w MRI sequence by 2 radiation oncologists reviewed by a neuroradiologist. The Region of interest (ROI) were: the surgical cavity +/- post-surgical residual mass (CTV_cavity); the CTV a margin of 1.5 cm added to CTV_cavity and the CTV_Ring volume resulting from subtracting the CTV_cavity from the CTV. Radiomic analysis and modelling were conducted in RStudio. Z-score normalization was applied to each radiomic feature.

A radiomic model was generated using the 226 features extracted from the CTV_Ring to perform a binary classification and predict the PFS at 6 months (statistical, morphological and textural features). A 3-fold cross-validation repeated five times was implemented for internal validation of the model.

Results: 270 ROIs were contoured. The proposed radiomic model was given by the best fitting logistic regression model, and included the following 3 features: F_cm_merged.contrast, F_cm_merged.info.corr.2, F_rlm_merged.rlnu. A good agreement between model predicted probabilities and observed outcome probabilities was obtained (p-value of 0.49 by Hosmer and Lemeshow statistical test). The ROC curve of the model reported an AUC of 0.78 (95% CI: 0.68 – 0.88) (Figure 1).

Conclusion: This is the first hypothesis-generating study who applies a radiomic analysis focusing on healthy tissue ring around the surgical cavity on post-operative MRI. This study provides a preliminary model for a decision support tool for a customization of the radiation target volume in GBM patients in order to achieve a margin reduction strategy.

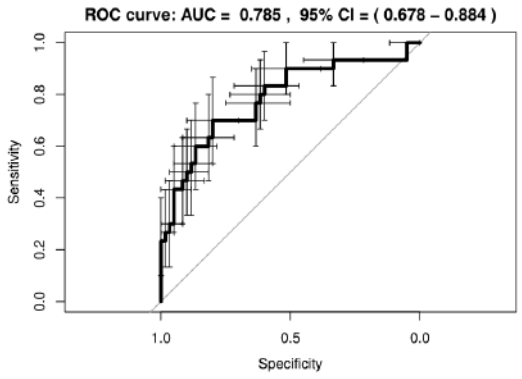

Figure 1.

P004

ROLE OF PERITUMORAL ZONE (PTZ) IN RELAPSING HIGH GRADE GLIOMA AND RE-IRRADIATION MODALITIES

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Aims: Despite the use of a multidisciplinary approach, after a relatively short period of time, almost all glioblastomas multiforme (GBMs) relapse within the high dose radiation field, defined as peritumoral brain zone (PTZ), needing a second treatment. Since this recurrence tendency carries important implications in the planning of external beam irradiation, in the aim to identify the best therapeutic decision, the current knowledge about PTZ, relapsing GBM and re-irradiation is summarized.

Method: Basing on literature data, several key factors have been individuated to explain the GBM tendency to recur near the initial pre-surgical tumour bed and the related radio-resistance (Table 1). Therefore, since this phenomenon supports the rationale for post-operative treatment with partial brain irradiation rather than whole-brain irradiation, different radiotherapy (RT) modalities, dose and fractionation options have been investigated to tailor the treatment to every single patient, balancing the benefits with the risk of toxicity.

Tables 1-2-3.

Table 1

Key factors	Mechanism	Reference
Microenvironment	Microenvironment is anatomically compartmentalized in tumor niches, where the signaling arising in stromal and tumor cells converges and regulates tumor progression and proliferation	*Colabrese, C. et al*
Hypoxia	Hypoxia-inducible factors (HIFs) have been shown to contribute critically to GBM tumorigenesis by regulating the tumorigenic capacity of glioma stem cells	*Li, Z. et al*
Metabolic alteration	Altered cellular metabolism is involved in dysregulated proliferation, resistance to cell death, angiogenesis, and invasion	*Libby, C. J. et al*
Glioma Stem Cells	Self-renewing tumorigenic cells able to propagate as therapy-resistant cells	*Kim, Y. et al*
Tumor heterogeneity	Different cell populations response to RT induces radioresistant populations dominance	*Voss, R. J. et al*
	MGMT methylation status can alter the motility and migration pattern of GBM cells	*Brandes, A. et al*
Micro-RNAs	Micro-RNAs have been shown to effectively regulate radiation-related signal transduction pathways in GBM	*Moskwa, P. et al*
DNA repair pathways	PI3-kinase/Akt, JAK/STAT, Wnt signaling pathway are involved in radioresistance	*Wang, J. et al*

Table 2

Technique	Indications	Schedules	Reference
Stereotactic radiosurgery (SRS)	SRS is an alternative to open surgery in selected patients with small tumor volume (<10 mL).	12-15 Gy x 1 fx EQD2 < 65 Gy	*Kong, D.S. et al*
Conventionally fractionated stereotactic technique (CFTR)	CFRT is indicated for larger tumors or tumors located close to eloquent structures (optic pathway, basal ganglia, motor or speech area). Fractionation has the radiobiological advantage to improve the therapeutic ratio.	1.8-2 Gy x 30-33 fx EQD2 < 36 Gy	*Scoccianti, S. et al*
Hypofractionated stereotactic radiotherapy (HFRT)	CFRT and HFRT are similar, but HFRT is completed in a shorter time, and improves the quality of life in patients with poorer prognosis. Moreover, dose escalation might have some potential benefits in surmounting local recurrence.	3-7 Gy x 5-10 fx EQD2 < 50 Gy	*Liao, G. et al*

Table 3

Technique	Indications	Schedules	Reference
Proton beams radiotherapy (PBRT)	Its better dosimetry allows safe irradiation of a large median PTV with high doses, sparing the surrounding organs at risks	9 Gy x 15 fx	*Lautenschlaeger, F.S. et al*
Carbon Ions radiotherapy (CIRT)	It's characterized by a low incoming dose and a majority energy deposition to a single point (Bragg Peak), beyond which the energy declines sharply	2.2 Gy x 21 fx	*Saeed, A.M. et al*

Results: The most used modalities are conventionally fractionated stereotactic radiotherapy (CFRT), hypofractionated stereotactic radiation therapy (HFRT) and stereotactic radiosurgery (SRS), characterized by different schedules (Table 2). The choice of fractionation must be individualized, basing on the volume of the target, the risk of toxicity and the performance status of the patient. Generally, radiosurgery is a choice for small lesions, hypofractionated stereotactic radiotherapy is feasible for medium lesions, while conventionally fractionated treatment is used for reirradiation of large lesions. Since GBM generally relapse within the high dose radiation field (PTZ) the dosimetric advantage of new beam qualities,

such as proton beams and carbon ions radiotherapy can be exploited (Table 3).

Conclusions: Even though the damage of normal brain tissue previously irradiated is a reason for concern for radio-oncologist, RT currently represents a feasible local approach to use as an alternative or in addition to surgery for recurrent GBM. The available evidence suggests that re-irradiation provides encouraging disease control and survival rates, and in some cases it is related to a significantly reduced risk of death.

P005

ARE THERE ANY BASELINE BLOOD VALUES WHICH CAN BE PREDICTIVE OF CLINICAL OUTCOMES IN ADENOID CYSTIC CARCINOMAS (ACCS) TREATED WITH CIRT?

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Background: In the last years there has been an emerging interest in the predictive role of blood biomarkers in oncological patients (pts). Literature data reported better clinical outcomes for patients with lower neutrophil to lymphocytes ratio (NLR) as well as haemoglobin (Hb) values between 12-14 g/dL for women (W) and 13-15 g/dL for men (M), associated with a maximum oxygenation status. Their significance remains to be established in adenoid cystic carcinomas (ACCs) treated with carbon ion radiotherapy (CIRT).

Methods: We retrospectively analysed the data of 49 consecutive head and neck ACC pts treated with CIRT (total dose: 57.6 GyE-68.8 GyE/12-16 fractions). The correlations between potential blood biomarkers were tested using the Spearman correlation coefficient. A subset of biomarkers was selected based on collinearity issues and literature data hence their significance was investigated using univariate Cox regression model concerning survival outcomes. Biomarkers' cut-off points were defined maximising the significance for disease-free survival (DFS) and tuned with regards to available literature data and clinical practice. Biomarkers' hazard ratios (HRs) were adjusted with a multivariable Cox model, based on the backward elimination method.

Results: The median follow-up was 34 months (IQR: 45 months; range: 3–76 months). There were 29 (59%) W and 20 M (41%); the median age was 53 years (IQR: 18,74 years; range: 22,3–78,6 years). NLR, absolute number of monocytes (ANM), glycemia and Hb were evaluated considering the following thresholds: 2,5; $0{,}4\times10^9$/L; 120 mg/dL; 14 g/dL. Univariate Cox analysis reported statistically significant HRs for Hb, with respect to DFS [3,38 (95% CI: 1,43–7,96, p=0,005], metastasis-free survival (MFS) [3,69 (95% CI: 1,23–11,07, p=0,02)] and overall survival (OS) [7,39 (95% CI: 1,77–30,91, p=0,006)], although NLR>2.5 was associated with a worse DFS (HR: 2,10, 95%CI: 0,85–5,08; p=0,11). NLR [5,87 (95% CI: 1,76–19,49, p=0,0039]) and Hb [3,31 (95% CI: 1,29–8,47, p=0,013)], appeared significantly associated with DFS adjusted for margin status at multivariable Cox analysis with Bonferroni correction. No significant results were reported in multivariable Cox analyses for LC and MFS, while for OS, Hb was the only significant parameter.

Conclusions: pts with a baseline NLR>2.5 and Hb>14 g/dL showed a worse DFS; baseline Hb<14 g/dL was related to a better OS. Validation in a larger prospective cohort is warranted.

P006

TREATMENT TIME ANALYSIS FOR HALCYON LINEAR ACCELERATOR: HOW MUCH FASTER CAN WE GO?

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Aims: The Varian Halcyon accelerator could potentially speed up radiotherapy sessions without a loss of the treatment quality respect to conventional linear accelerators. Treatment setup benefit of the availability of external light-markers and of a simplified and guided workflow. The time dedicated to IGRT can be reduced by fast CBCT acquisition. Higher maximum speeds of gantry and MLC allow to reduce VMAT beam-on time. This study aims to compare treatment time between Halcyon and other linear accelerators and to quantify the time saving.

Method: Treatment time (TT) and delay time (DT) on three linear accelerators – Halcyon (H), TrueBeam (TB), 2100 DHX (DHX) - were retrospectively, systematically and anonymously acquired during the first year of Halcyon activity using InSightive Analytics (IA) software

for the following treatment sites: head and neck (H&N), breast, prostate, rectum and gynecologic. TT was recorded as the time between opening and closing of each radiotherapy session at the treatment console. DT was acquired as the differences between activity scheduled start and the actual time of session opening. TT and DT were statistically compared between each pair of accelerators using Mann-Whitney non parametric test. Percentage differences of median treatment time $\%_{TT}$ and median delay time $\%_{DT}$ of H with respect to TB and DHX was evaluated.

Results: Using IA software, a total of 2159, 9011, 3196, 869 and 1005 treatment fractions were retrospectively and systematically recorded for H&N, breast, prostate, rectum and gynecologic respectively during a period of three months. Median [25-75 percentiles] Halcyon TT were 10.3m [8.7-14.6]m for H&N, 10.1m [8.4-14.0]m for breast, 9.6m [8.1-12.9]m for prostate, 10.5m [8.8-14.3]m for rectum, 12.5m [9.2-24.4]m for gynecologic. For all anatomical sites, a statistically significant reduction ($p<<0.001$) of both TT and DT was obtained for H compared to both TB and DHX linear accelerators. $\%_{TT}$ using H were 38% (TB) and 49% (DHX) for H&N, 43% (TB) 49% (DHX) for breast, 48% (TB) 56% (DHX) for prostate, 46% (TB) 38% (DHX) for rectum, 28% (TB) 28% (DHX) for gynecologic. $\%_{DT}$ using H were 25% (TB) and 50% (DHX).

Conclusions: Halcyon is able to drastically reduce the both TT and DT for all investigated anatomical sites. Despite of the relatively short observation period, InSightive Analytics software allowed for a systematic, large-population analysis which was characterized by an high level of statistical significance.

P007

MANAGEMENT OF RADIOTHERAPY TREATMENT INTERRUPTIONS: PRELIMINARY RESULTS FROM A NATIONAL SURVEY

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Aim: Radiotherapy (RT) overall treatment time is one of the most important predictors of treatment effectiveness, being associated with greater local control and impacting overall survival. Due to the limited literature data about the management of RT interruptions, a national survey (May 1-June 15, 2022) was conducted to investigate the Italian status of art.

Material Method: Directors of RT Centers were invited to take part in a survey focusing on: the number of days per week of RT treatments; the management of RT interruptions; the use of guidelines for the management of RT interruptions.

Results: The survey was completed by 85 (46.4%) radiotherapy centers (Figure 1). Respondents' median age was 57 years (range 41-74). The average number of LINACs was 2 (range 1-6), and 4 of the 85 centers conduct clinical activities 6 days per week, while the remaining have them 5 days per week. The vast majority (97.6%) of centers expressed interest in the survey topic, considering interruptions a critical issue to be able to manage, particularly for patients who received radical RT for head and neck, cervix, lung and rectal cancer. 71% of respondents were of the opinion that a 5-day or longer interruption could have an impact on the outcome of RT. 24 Centers (28%) declared to follow some international guidelines for management of interruption, whereas 17 centers (20%) had own guidelines. The most frequent causes of interruptions in the various centers were ascribed to LINAC breakdowns (54%), toxicity (21%), or patient compliance (13%). In the event of a LINAC breakdown, 65 centers declared that patients would be treated in the other one without doing a recalculation for the second machine in 19 of the 65 centers. The survey also documented a behavioral shift between the pre-vaccination period Covid19, when 33 centers declared to discontinue a positive patient until a negative Covid-19 test, and the post-vaccination period, when only 18 centers declared to discontinue a positive patient until a negative Covid-19 test. Most of the centers (85%) compensate / recover the lost dose by increasing the total dose (82%), recovering on Saturday (33%), performing 2 daily sessions (18%), using an accelerated regimen in the final part of the treatment (17%). Only 21 centers (25%) recover dose constantly.

Conclusion: Heterogeneity in RT interruption management emphasizes the importance of national guidelines/society recommendations.

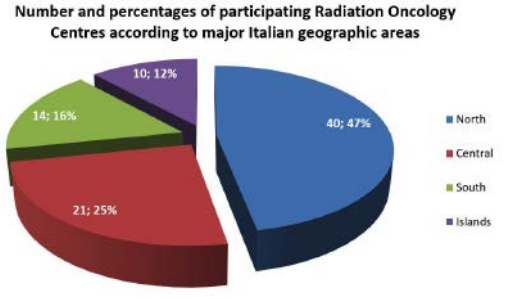

Figure 1.

P008

RESPIRATORY MOTION TRACKING AND PATIENT IMMOBILIZATION FOR STEREOTACTIC RADIATION THERAPY. A MONOISTITUTIONAL CASE STUDY

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Aims: Stereotactic body radiation therapy (SBRT) is a radiation therapy technique that delivers a high dose of radiation very precisely to an extracranial target, using either a single or a small number of fractions. Given the high doses and the potential organ motion, an accurate immobilization and a 4D CT acquisition system are required. The aim of this study is to analyze our data about reproducibility and correct execution of the treatment after patients'respiratory training, and using specific immobilization system and 4D CT.

Methods: We retrospectively analyzed data regarding 79 patients treated with pulmonary and upper addominal SBRT from October 2019 to May 2022. Patients were routinely positioned based on skin marks and with personalized abdominal compression with a polystyrene structure. Each patient received adequate respiratory training and the mask packaging was carried out in the forced expiration phase. CT simulation have been acquired, using a respiratory gating system for tracking patient's normal respiratory cycle based on a camera and optoelectronic markers positioned upstream of the abdominal compression. We analyzed the images using a four dimensions (4D) software to accurately correlate the shift of the tumor with the breathing motions. Target volume has been defined by the envelope of all different position of the lesion during breath cycle; before radiation delivery, position correction was performed via cone beam CT.

Results: The respiratory tracing system revealed significant organ motion only in 4/79 cases; in the rest of the patients there weren't significant variation during respiratory cycle, demonstrating the excellent positioning and compression system. The CBCT carried out before the treatment never showed target missing.

Conclusion: Our experience testifies how the tracing of the respiratory cycle can be correlated with adequate / inadequate respiratory education of the patient and an excellent immobilization. This is a path that can be followed in the hypothesis of reducing acquisition costs and times, reserving respiratory tracking during treatment for the few cases when immobilization and patient compliance can be not adequate.

P009

IMAGE GUIDED RADIOTHERAPY (IGRT) IN LOMBARDY: A SURVEY BY THE LOMBARDY SECTION OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Introduction: Image guided radiation therapy (IGRT) has changed clinical practice. In 2016, AIRO has published practical recommendations for the use of IGRT. Nevertheless, there are still many differences between Italian centres. In the last few months, we proposed this survey to Radiotherapy Centres in Lombardy to picture the current clinical practice use of IGRT.

Material and Methods: In 2021, during the meetings of the regional executive committee of AIRO Lombardy, a questionnaire was drawn up on the use of IGRT. The survey consisted of 32 multiple choice, divided into 5 topics: type of hospital, patients treated in 2019, number of LINACs; presence of protocols for IGRT management and staff involved; IGRT in stereotactic treatments; IGRT in non-stereotactic treatments; availability of medical and technical staff. The survey was sent by e-mail in August 2021 to all the Directors of the Radiotherapy Centres in Lombardy, with reference to the data of 2019. The analysis was carried out with the data collected in December 2021.

Results: 27 Directors answered to the survey (77%). 85% of the centres have an IGRT integrated device on all available LINACs. The most used IGRT modality (92%) is CBCT). Daily IGRT control is favoured for prostate (100%), head and neck (87%) and lung (78%) neoplasms. Most centres (74%) have produced protocols to ensure uniformity in the IGRT process. Only in 10 centres there is training with CME for staff, while the remaining departments had a training based on "experience". The Radiographers (RTTs) do not perform any type of IGRT control in 6 cases (22%), only for some districts in 12 cases (44%) and always in 9 cases (33%). If RTTs perform IGRT, a RO is present in real time, in most cases. All the Directors have expressed a desire to exploit RTTs' skill for performing the IGRT procedure, although 81% of them would still like to maintain supervision.

Conclusions: IGRT can nowadays be considered standard practice in Lombardy. IGRT is of paramount importance to achieve high-quality treatments. However, it comes at the price of more time consuming procedures and requires accurate planning of the activities of the different professionals involved. A balance between a fully physician-controlled process and an increased role for specifically trained radiographers is actively searched for.

P010

THE LESSON FROM COVID-19 PANDEMIC IN BASILICATA: RADIOTHERAPY GIVE ME FIVE

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Aims: The five fractions radiotherapy (RT) is well acknowledged for the treatment of prostate, breast and rectal cancer, showing better survivals outcomes and a quite different toxicity from the standard fractionation. From Covid-19 pandemic, hypofractionated radiotherapy has been delivered as per guidelines to reduce patient's accesses to the hospital. At the same time, this approach has been found easy in solving the logistic problems of this region like own guide avaibility for older patients or great distances and transfer from the suburbs of Basilicata to our Centre. We report our experience in regard with quality of life due to this treatment choice.

Methods: Five fractions hypofractionated radiotherapy was delivered in 122 patients from January 2020 to April 2022, including 51 patients with early breast cancer (BC), 33 patients with low grade prostate cancer (PC) and 40 patients with advanced rectal cancer (RC). Ultra-hypofractionated radiotherapy was given as follows: 5,2 Gy/ 26 Gy for BC ; 5 Gy / 35 Gy day off and day on in PC; 5 Gy/ 25 Gy in RC. Mean age was 70 years (65-80). No acute toxicities were recorded. During the first follow up, a questionary regarding the compliance to this treatment was delivered according the EORTC QC30. Questions assessed the quality of life during the week of treatment. At least patients were asked to answer to the compliance to treatment was as follows: not at all (1), a little (2), quite a bit (3), very much (4). Analysis was stratified in terms of age, sex, distance from the RT Centre and availability of own transfer.

Results: A good score was recorded for quality of life in 60% of patients. For compliance, the score 4 was defined by 70 % of patients. Females were 40%. Among them 60% were older than 70 years; 40 % had no own guide and 20 % no own transfer. Interestingly all of them lived in Centre over 50 kms far from the hospital. This treatment was considered to be strongly recommended.

Conclusions: During Covid-19 pandemic the hypofractionated radiotherapy has emerged as a necessary approach to treat patients and minimize infections. However, from this experience this approach has solved the well acknowledged problems of Basilicata radiotherapy: the distances and the transfers issues with a positive impact on quality of life.

P011

HOW THE COVID PANDEMIC AFFECTED THE LECCO RADIOTHERAPY DEPARTMENT

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During the year 2020, the Lecco hospital was devastated by the COVID pandemic, hosting more than 500 positive patients out of 700 total available places. Most of the activities were aimed at positive patients. The radiotherapy department continued its activities regularly, also giving support to the rest of the hospital. We studied the activity of our department, considering the number of patients treated year by year from 2016 to 2021, considering whether there were any changes in pathologies, patients number or treatment modalithy.

Data and methodology: From 02/19 to 10/19 the department worked with only one LINAC for equipment replacement. From 15/03/2020 a doctor was assigned daily to COVID departments and a TSRM moved to another service for clinical needs. From 09/2020 the doctor returned, the doctor in specialization school ended his period in our department and was not replaced. The TSRM has not yet been reassigned. Hours of service decreased from 10 (2018) to 7.15 hours(2020) due to TSRM numerd (7 total) . Ttere was no change in the distribution of patients by pathology. Patients number was 649 in 2016; 693 in 2017; 728 in 2018 (10 hours) 617 in 2017 (12 hours) 736 in 2020 (7.15 hours) and 690 in 2021. In 2020, we treated also 45 COVID positive patients. With the new LINAC we have increased the number of VMAT - IMRT treatments with a reduction of 3DCRT treatments to from 75 to 20%. To increase treatments by reducing access, we have modified the fractionations, in particular for breast neoplasms and symptomatic patients. We have gone from 75% of breast treatments with conventional fractionation to 75% of patients with hypofractionation, 3% of patients with ultraIpo. For symptomatic patients, the treatment of choice involved the use of 1, 2 or 4 fractions in 92% of cases compared to 60% in 2016

Conclusions: COVID has changed the choice of fractionation, making it possible to maintain a high level of treatments, reduce patient access during that critical moments, keeping high the number of treated patients.

P012

ULTRAFRACTIONATED RADIOTHERAPY ADOPTION FOR BREAST CANCER AS TIME- AND COST-SAVINGS STRATEGY IN CLINICAL ONCOLOGY: A PROJECTED ANALYSIS OF THE RADIATION ONCOLOGY UNIT OF AREZZO-VALDARNO

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Aims: To evaluate the potential impact of use of ultrafractionated RT in five fractions according to FAST FORWARD trial (as suggested by the recently published ESTRO-ACROP recommendations) in terms of reduction of delivery costs and treatment times.

Methods: We retrospectively reviewed patients treated with adjuvant RT for breast cancer in 2021 at the Radiation Oncology Unit of Arezzo-Valdarno, registered in our management information system (Mosaiq®-Elekta®). The cost and course of breast RT for conventional, hypofractionated and ultrafractionated regimens were calculated using the Regional Radiotherapy Cost Estimator of Tuscany. The potential annual cost savings and decrease in number of accesses at the Radiation Oncology Units were estimated, assuming that 26 Gy in five fractions according FAST FORWARD trial was used for non-nodal breast or chest wall (without reconstruction) RT.

Results: In 2021, 167 BC patients were treated at the Radiation Oncology Unit of Arezzo-Valdarno. Of them, 6% received post mastectomy RT (PMRT) and 94% whole breast RT (WBI). Standard fractionation was used for PMRT (50 Gy in 25 fractions) and/or regional node irradiation (RNI), hypofractionation (40 Gy in 15 fractions) was delivered in almost all cases of WBI, except for 4 cases treated with ultrafractionation (26 Gy in 5 fractions). Electron boost to surgical bed was added in 19,1% of cases (10-15 Gy in 4-6 fractions according to surgical margins and indications reported in ASTRO consensus). 2998 fractions of adjuvant RT for BC patients were delivered, which would have corresponded to 879 fractions if ultrafractionated RT had been used, with a calculated reduction of 70,3% in number of fractions. The cost of BC RT courses in 2021 calculated according to the Regional Radiotherapy Cost Estimator of Tuscany was 218.005 euros. The projected potential maximum cost savings with full ultrafractionation implementation were estimated in 160.923 euros (-73,8%).

Conclusions: Our findings demonstrated that adopting the ultrafractionated regimen for WBI and PMRT can result in substantially reduced delivery costs and number of treatment times without compromising quality and oncological efficacy of treatment strategies, thus increasing the opportunity of equity of access to health care for all population.

P013

RADIOTHERAPY (RT) TREATMENTS IN PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIEDS), USING FLATTENED AND FLATTENING FILTER FREE (FFF) BEAMS

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Aims: The number of patients (pts) undergoing CIED implantation is growing. RT photons can potentially cause device malfunctions, especially for energy beams>18MV and dose to device >10 Gy. The purpose of this study is to evaluate the impact of RT on CIED in pts treated in our center

Method: The data of RT treatments of pts with CIED, performed at our center between 18/6/20 and 17/6/22 were analyzed retrospectively. 6MV photon beams (with and without flattening filter) from linear accelerators were used in the treatments. The technical characteristics of the treatment plans and the impact that RT had on the devices were evaluated. In our center, the protocol for CIED pts' management provides for an electrophysiological (EP) visit before the start of RT. The specialist assesses the status of the device and establishes the need to place a magnet on the device during the treatment delivery. During each session of RT, all pts are constantly monitored with audio-visual control and ECG by a trained nurse. In case of anomalies, the resuscitator is promptly asked to intervene. Each pt must undergo an EP check every 7 days during the treatment and at the end of it. Thereafter there are no routine checks, as the pts are redirected to the reference center

Results: We performed 40 RT treatments on 40 pts with CIED (32 Pacemaker (PM) and 8 implantable cardioverter-defibrillator (ICD). The CIEDs implanted came from different manufacturers. The average age of the pts was 76 years (44-86), 31 were men and 9 women. In no case the contralateral relocation of the device before starting the RT was deemed necessary. 17 treatments concerned chest, 14 abdomen-pelvis, 2 brain, 7 head-neck (H&N). The VMAT technique was used in all treatment plans. The doses delivered ranged from 8 to 72 Gy and the doses/fraction from 2 to 10 Gy. The median dose to the CIED was: 0.21 Gy (0.04-3.45 Gy), the only 3 cases with a dose>2 Gy were 2 H&N treatments and 1 breast + supraclavicular region. In 17 plans the dose to the devices was not assessed because they were distant from the target. None out of the 40 treated cases reported malfunction

either during or at the end of RT.

Conclusions: A CIED dose lower than 3.5 Gy and the use of 6MV seem to be safe for the RT treatment of pts with CIED. The most important features in CIED pts' RT treatments are the expertise of the center and the multidisciplinary management of the patient, with the involvement of electrophysiologist, radiation oncologist, medical physicist, and nurse.

P014

RADIOTHERAPY TECHNOLOGICAL EQUIPMENT IN VENETO, ITALY: AN UPDATED REPORT FROM THE RETE RADIOTERAPICA VENETA

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Aims: Radiotherapy is an integral part of oncological comprehensive cancer management. It represents a cost-effective treatment if compared to surgery or chemotherapy though purchase of radiotherapy equipment implies notable investments from financial and technical point of view. As reported in literature, the number of megavolt units per million inhabitants is a viable indicator to quantify radiotherapy resources and geographical disparity in the access to radiation treatments. The present report is an assessment conducted among Radiation Oncology centers of Veneto region with the aim to collect updated information concerning radiotherapy assets and technological equipment.

Methods: Data concerning Veneto Radiation Oncology departments and radiotherapy activities were collected. In April 2022, a survey among Veneto radiotherapy departments was conducted to assess geographical layout of radiotherapy units and their obsolescence.

Results: Veneto accounts for ten Radiation Oncology departments and two satellites with an average number of two departments per million inhabitants. Veneto, to date of data collection in April 2022 was endowed with 1 megavolt unit for about 153,000 inhabitants, in particular a total of 29 linear accelerators (LINACs), two Helical Tomotherapy, and two dedicated stereotactic machines have been recorded. The number of megavolt machines per million inhabitants resulted to be 6.7. Five IORT and two brachitherapy units were also available. Particular attention was paid to the obsolescence of the equipment. In April 2022 the mean age of LINACs was 7 years, with 27% of treatment machines older than 10 years.

Conclusions: The assessment of standards of quality in cancer care is an issue of primary importance particularly in a country with a regionally based health service. Radiotherapy assets and equipment in Veneto seem to be appropriate to standards in terms of availability and technology. The periodic assessment of radiotherapy activities and facilities is essential to plan financial investments and pursue quality and equity in cancer treatments.

P015

USE OF GINGER MAUVE GRAPEFRUIT SEEDS AND SODIUM HYALURONATE DIETARY SUPPLEMENT DIETARY SUPPLEMENT (NAUGIN•) FOR RADIATION INDUCED ESOPHAGITIS MANAGEMENT: A PILOT STUDY

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Aims: Radiation esophagitis (RE) is inflammation of the esophagitis due to radiation. Radiation esophagitis is one of the most frequent side effects of radical, symptomatic, or prophylactic radiotherapy of the mediastinum particularly when treatment is delivered with concurrent chemotherapy. The onset of RE is very common in patients undergoing radiotherapy for breast, lung cancers and lymphomas. The aim of this prospective study is the evaluation of efficacy and safety of NAUGIN® supplementation in a series of patients with esophagus involved during radiation treatment.

Methods: From February to July 2021 we enrolled 16 patients, 3 (19%) males and 13 females (81%). Median age was 62.5 (range 37- 84) years. RT was delivered to lung cancer (n=4),25%, and breast cancer (n=12),75%. All patients underwent to radiotherapy (RT) with an exclusive modality (n=6),38%, or plus chemoterapy (CTX) (n=10),62%, 2 of these conchomitant, with radical or adjuvant intent. Average Total Dose of treatment was 52,5 (range 40-60) Gy. All patients received an esophageal mean dose according with constraints < 34 Gy. Average Maximal Esophageal Dose was 31 (range 14-65) Gy. All patients received Naugin 1(packet/die half hour

before lunch) at the start of RT and were evaluated with general quality of life and esophagitis specific questionnaires EORTC QLQ-C30; QLQ-OES18; FACT-G; FACT-E; RDQ.

Results: All patients performed EORTC QLQ-C30; QLQ-OES18; FACT-G;FACT-E;RDQ questionnaires at first day of RT and at 10 and at 30 days later the start of RT. The mean score for global health status QoL was 85. The mean value of the five scales of functioning ranged from 72 (emotional functioning) to 87 (social functioning). The highest symptom score on QLQ-C30 was for nausea and vomiting, followed by fatigue and pain. In the QLQ-OES18, speech, cough and taste problems ranked as the three worst symptoms of 10 items subgroup.

Conclusions: Quality of life is adversely affected in patients undergoing mediastinum radiotherapy for lung, breast cancer and lymphomas. Radiation esophagitis had an important impact in terms of decreasing quality of life. Naugin® may allow an improvement on RE related symptoms and on quality of life. More research is needed to address the gain of dietary supplement, Naugin®, in patients underwent to RT on mediastinum.

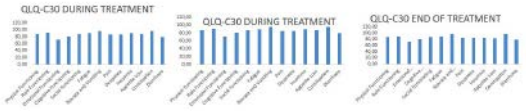

Figure 1.

P016

DISCONTINUOUS HYPOFRACTIONATED RADIATION THERAPY FOR TREATING BLADDER CANCER RELATED HEMATURIA

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Aims: Hematuria is described in approximately 85% of patients with bladder cancer, resulting the most frequent symptom. Hemostatic radiotherapy represents a valid alternative for palliative care in patients unsuitable for surgery and the most frequently used dose fractionation regimens are 30 Gy in 10 fractions (BED10=39 Gy), followed by 20 Gy in 5 fractions (BED10=20 Gy). However, the optimal schedule remains undefined and the most widely used fractions require the patient's daily and prolonged collaboration with adverse consequences on the patient's Quality of Life (QoL). Hypofractional radiotherapy (HFRT) may be able both to ensure a shorter duration of treatment resulting in less impact on QoL and more effective/quick in controlling hematuria. Herein we report our experience on using HFRT in 13 patients with bleeding bladder cancer by describing its benefits in symptomatological control and evaluating the limits of the date available in literature, and exploring the results of clinical trials and future directions

Methods: Thirteen patients, nine male and four female, with non-operable bladder cancer were treated with 23 Gy in 4 fractions, 6.5 Gy on days 1 and 3, followed by 5 Gy/fr on days 15 and 17. Centering Computed Tomography (CT) was performed at full bladder. Clinical target volumes (CTV) included the whole bladder, with an expansion of 1 cm for Planning Target Volume (PTV). Cone beam CT was performed at the beginning of HFRT and at each treatment session with the Hexapod system for corrections of the table rotation. The dose constraints were applied to meet dose criteria for target and OAR. The primary endpoint was the Hemostatic Control (HC) rate at the end of the radiation cycle. Secondary endpoints included mid-term HC, toxicities and over- all survival. Comparative analyses were performed by exact Fisher test with a cut-off of 0.05 for statistical significance.

Results: HC was obtained in all patients at the end of treatment with HFRT. Haemoglobin levels, well below normal before treatment, were normal at the end of HFRT. No acute or late gastrointestinal and/or genitourinary toxicity was reported.

Conclusions: According to data in literature, our experience suggests that "discontinuous" HFRT is fairly well tolerated, represents a effective alternative and offers a considerable benefit in terms of QoL for patients with bladder cancer.

P017

VITAT AUTOMATED PLANNING KNOWLEDGE-BASED MODEL OPTIMIZATION FOR RIGHT-SIDED WHOLE BREAST RADIOTHERAPY WITH HALCYON•

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Aims: To adapt a Knowledge-Based (KB)-automatic planning approach for right-sided (R) tangential fields (TF) whole breast treatment using the volumetric technique ViTAT (Virtual Tangential Arc Therapy) with 6MV FFF (Free Flattening Filter) on Halcyon (Varian).

Methods: An automatic KB-planning approach using

ViTAT was previously validated and implemented using 100 TF plans delivered by the TrueBeam Linac and trained by the RapidPlan tool (vs. 15.6, Varian). The clinical activation of the new Halcyon Linac, which uses only a 6MV FFF beam, highlighted the need to adapt the model to this new equipment. ViTAT plans were created on Halcyon for 25 patients. Plan optimization was fully automated through the previously developed optimization template, based on the KB-model. The resulting Halcyon plans show an unacceptably inhomogeneous dose distribution, due to the FFF beam. To make the dose distribution homogeneous, compensating for the effect of the FFF beam, we tested the effect of increasing the beam delivery angles from 20° to 30° and 40°. Also in these cases, we used fully automated planning. A comparison of the plans in terms of OARs/PTVs dose-volume parameters was made. Wilcoxon-tests were performed to assess statistically significant differences ($p<0.05$).

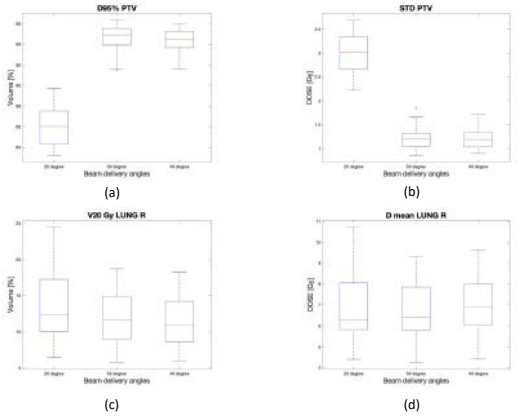

Figure 1.

Results: Plans obtained with beam delivery angles of 20° were all unacceptable in terms of PTV coverage (median D95%=86%), while the plans obtained by increasing the beam delivery angles to 30° and 40° were clinically acceptable (D95%=94.9% and 94.5% respectively). The homogeneity of the PTV dose distribution, through its standard deviation (STD), was significantly worse for the 20° plans compared to the 30° and 40° plans ($p<0.05$), while was not statistically significant between 30° and 40°. It is intriguing to note that DVH of the OARs does not undergo significant variations. Mean dose (Dm) and V20 of the right lung, were not significantly different (median V20<14%; Dm<7Gy). The heart (H) left breast (LB), and left lung (LL) showed low Dm (H<0.8Gy; LB<0.4Gy; LL<0.2Gy) with statistically significant differences only between 20° and 40°.

Conclusions: We proposed an approach to adapt the ViTAT technique using a 6MV FFF beam on Halcyon. Increasing the delivery angle from 20° to 30°/40° an optimal PTV coverage was obtained, maintaining similar sparing of the OARs. The adapted KB model ViTAT is currently used in clinical practice. Development and implementation of the KB model ViTAT for the left breast are ongoing.

P018

MAMETIC TRIAL: MANAGEMENT OF METASTATIC DISEASE IN CAMPANIA. A RETROSPECTIVE AND PROSPECTIVE MULTICENTER STUDY ON PALLIATIVE RADIOTHERAPY

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Aims: In the Italian Campania Region, 30.517 new cases of solid cancer have been diagnosed, in 2019. Of those, patients with metastatic disease are up to 20%. This class of patients is extremely diversified and the offer of radiotherapy may vary in different geographical areas within the region. The aim of this trial is to evaluate the occurrence of metastatic cancer patients candidates for

palliative radiotherapy in several areas and the management of the disease through radiation therapy. We present retrospective data to investigate the use of radiotherapy in this patient setting and especially to evaluate the local response to the patient's request.

Methods: We retrospectively evaluated patients enrolled with a diagnosis of metastatic disease in regional radiotherapy centers between January 2019 and July 2020. Considering regional epidemiological data, was expected an enrollment of 2500 patients. We evaluated the percentage of primary tumors in metastatic patients, percentage of metastatic patients treated with radiotherapy in the area of residence, percentage of patients with metastases at diagnosis and percentage of multimetastatic patients.

Results: We evaluated 2634 metastatic patients with a median age of 67 years (18-99) treated in 13 centers. 34% of them had primary lung cancer metastases, 19% primary breast cancer metastases, 10% primary prostate cancer metastases. The percentage of patients treated in their province of residence was 97% in Naples, 53% in Avellino, 68% in Benevento, 74% in Salerno, 22% in Caserta. The radiotherapy treatments made with an urgent request were performed in the province of residence only in Naples and Benevento. Of the patients evaluated, 15% were metastatic at diagnosis. 31% of patients were multimetastatic.

Conclusions: Our preliminary data show a migration between province of patients candidates for radiotherapy. It will be interesting with further analysis to understand the reasons for these choices. There are probably important differences in the therapeutic offer within the regional territory and this data can represent a starting point for future technological investments in the Region, with the aim of bridging territorial differences and guaranteeing adequate care for all patients.

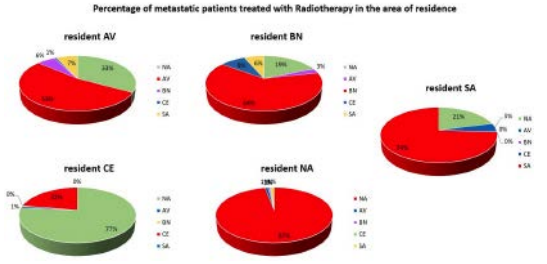

Figure 1.

P019

A PRACTICAL REPORT ON DOSE CONSTRAINTS IN BREAST CANCER HYPOFRACTIONATED RADIOTHERAPY

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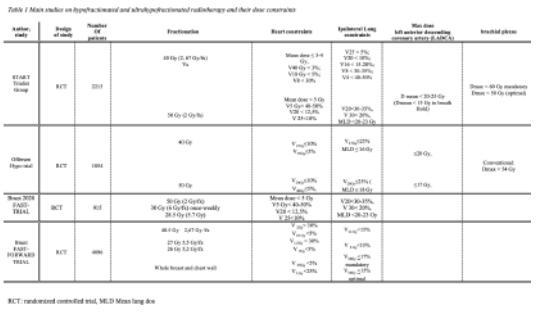
Aims: Adjuvant radiotherapy (RT) is a mainstay of breast cancer (BC) treatment. Moderate hypofractionation such as 42.5 Gy in 16 daily fractions or 40 Gy in 15 daily fractions is an effective and safe treatment in terms of local control and side effects for whole breast, chest wall and nodal irradiation with or without breast reconstruction. Moreover, ultrahypofractionated whole breast irradiation, delivered in five daily fractions to a total dose of 26 Gy, is non-inferior at 5 years in terms of local recurrence, and provides lower acute and similar late normal tissue effect rates compared with a moderate hypofractionated schedule. We reported organs at risk (OARs) dose constraints pocket in hypofractionation breast cancer RT for daily practical using.

Method: A review of the scientific literature was conducted in order to identify main studies about hypofractionated RT in BC. Then supplementary scientific papers about RT planning were analyzed to extrapolate the dose-constraints used. Dmean indicate mean dose of the volume, Vx the percentage of volume covered by dose value x and Dmax the maximum dose in an organ at risk volume. All studies reported dose-constraints for heart, ipsilateral lung while only two studies reported Maximum dose to left anterior descending coronary artery.

Table 1.



Results: Table 1 summarizes the planning data and represents our pocket for daily practical use for OARs dose-constraints in prescribing BC hypofractionation. About cardiac toxicity, Quantitative Analyses of Normal Tissue Effects in the Clinical (QUANTEC) guidelines

estimated a probability of <1% of cardiac mortality at 15 years for V25<10%. In moderate hypofractionation with 15–16 fractions of 2.6–2.7 Gy, is highlighted a lower radiogenic burden on heart structures as compared to conventional fractionation.

Conclusions: Changing this paradigm in breast cancer dose prescribing leads to benefits for patients, for radiotherapy centers and national health services, allowing for redistribution of insufficient resources, shortening of waiting times and overall improvement of departments' capacity. Attention must be paid to the new OARs dose-constraints and to take confidence about. We submitted an easily accessible and schematic report for hypofractionation breast cancer RT planning aimed for daily practical use.

P020

A PRACTICAL REPORT OF MAINLY USED DOSE CONSTRAINTS IN HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER

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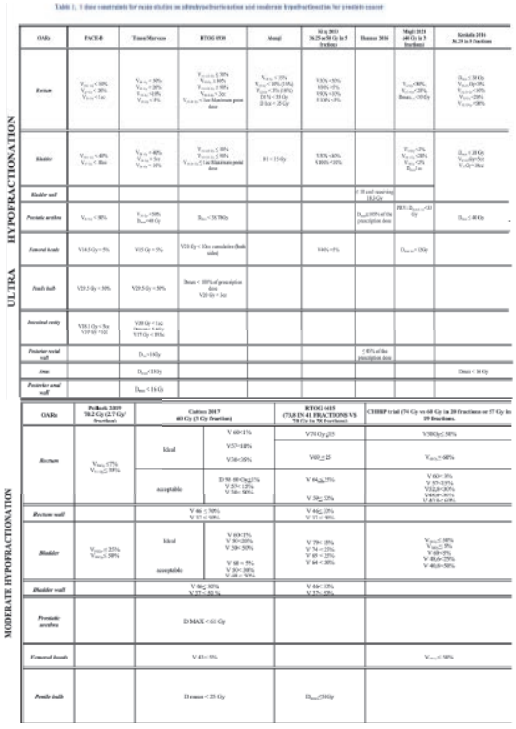
Aims: In prostate cancer External beam Radiotherapy (RT) affirmed as an effective treatment, with rate of local control equivalent to prostatectomy. In last decades, due to technical and Imaging innovations, a more selective and target conformed RT may be delivered. Furthermore, therapeutic ratio of hypofractionation is enhanced by the radiobiological characteristics of prostate cancer cells as reported in several randomized trials. Then a routinely prescription of hypofractionated schedules is increased in RT departments resulting in increasing of treatments capacity and reducing waiting lists. We report organs at risk (OARs) dose constraints pocket in hypofractionation prostate cancer RT for daily practical using.

Methods: We reviewed scientific literature in order to identify main studies using hypofractionated RT. Then supplementary scientific papers about RT planning were analyzed to extrapolate the dose-constraints used. Hypofractionation may be distinguished in two main schedules: moderate Hypofractionation with fraction size of 240-340 cGy and ultra or extreme Hypofractionation with fraction size> 500 cGy, according to ASTRO, ASCO, and AUA Evidence-Based Guideline. The prescription of hypofractionation schedule can be influenced by the ability to respect Organs at risk dose-constraints.

Results: In Table 1 are reported the main studies and related dose-constraints for pelvic organs at risk (OARs). Most studies offered dose values limits of dose for whole rectum, bladder and femoral head. Several studies have evaluated penile bulb, rectal, anal and bladder walls and prostate urethra.

Conclusions: Changing this paradigm in prostate cancer dose prescribing leads to benefits for patients, for radiotherapy centers and national health services, allowing for redistribution of insufficient resources, shortening of waiting times and overall improvement of departments' capacity. Attention must be paid to the new OARs dose-constraints and to take confidence about. We submitted an easily accessible and schematic report for hypofractionation prostate cancer RT planning aimed for daily practical use.

Table 1.



P021

MULTIDISCIPLINARY APPROACH TO CANCER CARE: WHAT RESOURCES?

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Aims: We aim to assess the gap between Sicilian Radiation Oncology(S-RO) Units and Oncology's ones in rapidly increasing of radiotherapy clinical workload.

Methods: Between February and March 2022 a questionnaire was sent to 16 S-RO and 25 Oncology centers. Data on following items were collected:staff members, hospital bed complements, day bed unit, LINACs and official multidisciplinary team meeting (MTM).

Results: Between February and March 2022, all S-RO centers and invited Medical Oncology (MO) centers filled the questionnaire with a response rate of 100%. At the time of the analysis the total number of S-ROist is 80 (range 3-9) of which 79 with permanent assignment and 1 with a fixed–term assignment. Only one center presents a postgraduate course (Messina) with 22 RO-resident and 1 Ph.D. A total of 35 LINACs are present throughout the region (mean of 2 LINACs for each radiation-center, range 1-4). One center present both a Brachitherapy source and a CyberKnife System; one center has a TomoTherapy System and only one collaborate with Neurosurgery Department for GammaKnife Radiosurgery. Conversely, the overall number of S-MOist is 193 (range 3-17), of which 181 with permanent assignment, 7 with temporany contract and 5 awarded an oncology-fellowship. 2 centers (Messina and Palermo) present a postgraduate course with 68 MO-resident.In MO wards a total of 460 hospital beds are available: 213 (range 6-24) for in-bed and 239 (range 1-19) as day-hospital beds. RO units have 6 operating hospital beds (4 in-bed and 2 day-hospital).The MTM were S-ROist and S-MOist are called to participate are 60 (range from 1 to 7, with a mean of 3 meeting for each center). It is noteworthy to underline that, according to AGENAS (Agenzia Nazionale per i Servizi Sanitari) prescriptions, to participate in a MTM every doctor has to dedicate at least the 40% of her/his activity in a single pathology (breast, lung, prostate, and so on).

Conclusions: Radiotherapy represent one of the main component in interdisciplinary cancer care; if we consider the ratio between necessary professional figures and workload, the minimum need for dedicated personnel is often not met.Here we demonstrate a great disparity in staffing between S-RO centers and MO one's.Finally, the low number of radiation oncologists per MTM could led to a significant clinical risk for oncologic patients. Therefore, we suggest to improve resource planning to overcome inequalities and provide optimal care for cancer patient.

P022

NEEDS OF PATIENTS UNDERGOING PROTON THERAPY: A SURVEY CONDUCTED IN 10 EUROPEAN CENTRES

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Aims: Proton therapy (PT) centres are still few in number, and the access to treatment could be characterized by patients' logistic and economic challenges. The aim of this study is to assess the support provided to patients undergoing PT in 10 PT facilities across Europe.

Methods: Through a personnel contact, an online questionnaire (62 multiple-choice and open-ended questions) via Microsoft Forms was administered to Medical Directors of 10 PT centres in Europe. The survey was composed of general queries about the clinical activity (questions from 7 to 35), while 2 further sections were dedicated to the patients' logistic and economic challenges in accessing PT and investigating the possible offered reimbursements. All of the respondents gave their consent to the use of data for scientific purposes.

Results: The proposed online questionnaire was completed by all 10 centres from March to May 2022; with 9 centres treating from 100 to 500 patients in the last year. In 2021, paediatric patients accounted for 10-30%, 30-50% and 50-70% of the entire cohort of treated patients for 7, 2 and 1 centre, respectively. More than 10% of all patients came from outside the country in 40% of the cases. The most frequent tumours treated are brain tumours, sarcomas and head and neck carcinomas; in all centres, the mean duration of PT is more than 3 weeks and in 70% of cases patients rent an apartment for the whole duration of the treatment. In 80% of cases, the treatment reimbursement is supplied by the respective country's Health National System (HNS); moreover, HNS provides economic support in 60% of centres, while logistic support is provided in only 20% of centres. Conversely PT facilities, offers economic and/or logistic

support in 80% of the cases. However, in the majority of the centres, patients do not receive any support for meal costs. A summary of these results is presented in Table 1. Overall, 70% of respondents agree that geographic challenges could limit a patient's access to proton facilities, although economic and accommodation-related discomfort do not seem to have a relevant impact. Finally, 60% of respondents believe that patients should be given general additional support in case of indication to PT.

Conclusions: Relevant national disparities in supporting patients referred to PT have been revealed in 10 PT facilities across 9 different European countries. This aspect could lead to an unequal access among patients receiving indication to PT.

Table 1. Graphical representation of support to patients provided by Health National System and/or PT Institutions. Legend: 1. Belgium; 2. Italy; 3. Italy; 4. France; 5. Netherlands; 6. Denmark; 7. Germany; 8. Austria; 9. Sweden; 10. Spain. Note: Meals are covered by regional councils in Sweden (n. 9).

	Center ID									
	1	2	3	4	5	6	7	8	9	10
Economic support from the Health National System for patients' accommodation	✗	✗	✗	✗	✓	✓	✓	✓	✓	✓
Logistic support from the Health National System for patients' accommodation	✗	✗	✗	✓	✗	✓	✗	✗	✗	✗
Logistic support provided by the Health National System for parents of pediatric patients	✗	✗	✗	✓	✗	✓	✗	✗	✗	✗
Support provided by the Health National System for meal	✗	✗	✗	✗	✗	✓	✗	✗	✗	✗
Economic/logistic support from your Institute for patients' accommodation	✗	✗	✓	✓	✓	✓	✓	✓	✓	✓
Support provided by your Institute for meal	✗	✓	✗	✗	✗	✗	✗	✗	✗	✗

P023

SMILEINTM TOTEMS IN RADIOTHERAPY: PATIENTS' SATISFACTION IN CRITICAL SCENARIOS OF LIMITED EQUIPMENT AND COVID-19

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Aims: Radiotherapy (RT) cannot be deferred for about 50% of cancer patients. Technological obsolescence and reducted equipment can negatively impact on perception of RT quality and timeliness. COVID-19 pandemic produced an important distress on health care. We report a mono-institutional experience on patients perception of quality assessment in our department through RAMSI (Radiotherapy Amica Mia—SmileINTM (SI)—My Friend Radiotherapy SI) project in critical scenarios of limited equipment and COVID-19.

Methods: "Patient-reported experience measures" (PREMs) have been divided in the following four questions: "Patient-centric welcome perception" (PCWP), "Comfort", "Professional skills" and "Punctuality". Patients could give their anonymous feedback, using HappyOrNot technology through face icon buttons on four totems located in strategic areas for patient flow within the Center. An internal benchmark was obtained using received feedback for each selected issue, after a preliminary observation period defined as reference. The SI Experience Index was collected, analyzed and compared. Weekly and monthly reports showing overall trends were generated for evaluating patient responses (Figure 1).

Results: Since February 2019 to February 2022, a total number of 8,924 patient accesses have been registered to our department; 17,464 daily treatments were recorded. A total of 5,803 feedback items were collected: 896, 1.267, 1.125, 2.542 for "PCWP", "Comfort", "Professional skills" and "Punctuality" respectively. An analysis of a period with the dismission of one LINAC was performed: only a reduction of SI index score and of Smile-in approved percentage was noted before LINAC decommissioning, due to continuous breakdowns, with an improvement of SI and Smile-in approved after this period. Also a COVID-19 time was analyzed with an uninterrupted continuity of radiation treatment courses: a mild decrease in evaluations was observed, in particular regarding PREM's "Welcome", "Comfort" and "Punctuality" (SMILE-IN Approved Δ-value: -9%, -3% and -4% respectively), while "Professional skills" resulted less affected (Smile Index Δ-value -0.1 and SMILE-IN Approved Δ-value -1%).

Conclusions: RAMSI project resulted effective to assess quality and timeliness of treatments perception, allowing to improve clinical procedures and treatments with corrective actions specially in critical scenarios of limited equipment and COVID-19. RAMSI project is currently ongoing in our Department.

Figure 1. Example of a monthly report of patient-reported experience measures (PREMs), SmileIN-approved and SI Index showed inside the department and available for the patients and clinicians.

P024

STEREOTACTIC BODY RADIOTHERAPY IN PANCREATIC CANCER: AN UPDATE OF A NATIONAL SURVEY BY THE AIRO GASTROINTESTINAL STUDY GROUP

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Aims: The role of stereotactic body radiation therapy (SBRT) is intensively investigated in pancreatic cancer, thanks the advantages of a short overall treatment time and potentially ablative doses. Since a great variability about indications and doses were reported before ASTRO guidelines publication, in October 2018 the AIRO study group of gastrointestinal malignancies proposed a national survey aiming to investigate this scenery. Currently, a new treatment paradigm is emerging, with a gradual transition from standard to ablative dose radiotherapy. Aiming to assess how the Italian centers have adapted their clinical practice to these changes, an update of the survey has been carried out.

Methods: The questionnaire was sent-back to all 22 Italian Institutions performing pancreatic SBRT and previously joined the survey.

Results: Three centers (14% *vs* 10% in 2018) treat more than 20 pancreatic cases/year and 32% (vs 18%) between 10 and 20 cases/year. SBRT is performed for unresectable locally advanced pancreatic cancer (LAPC) in 100% and/or for neoadjuvant treatment in borderline resectable (BR) disease in 50% of the centers (Figure 1). In 2018, although 60% of the centers delivered a 5-fraction schedule with a total dose of 25-30Gy, for both LAPC and BR disease, a large variety of fractionation schemes was reported. Currently, the 5-fraction is confirmed as the most used schedule, with an increased total dose range up to 30-40 Gy in the 73% of the centers for LAPC and in the 77% for BR patients. In the 81.8% of the centers the optimal prescription isodose level was between 85-95%, with a heterogeneity dose between 110-120%. Dimensional criteria (>5cm) and tight margins to adjacent structures were the major limiting factors for dose prescription in 63.64% and 100% of the center, respectively. In all centers SBRT is delivered during a chemotherapy interval. Concomitant chemotherapy is administered only in clinical trial in one center. When SBRT is administered after chemotherapy, a pause of 2-3 weeks or of one week is respected by the 35% and 20% of the centers, respectively.

Conclusion: SBRT has found a wide indication for LAPC and BR disease. Our analysis shows that highly effective doses are currently administered according to the available guidelines. Since a certain dose variability remains, a prospective multicenter study could be promoted to evaluate the most effective schedule and the best integration with the systemic therapies currently in use.

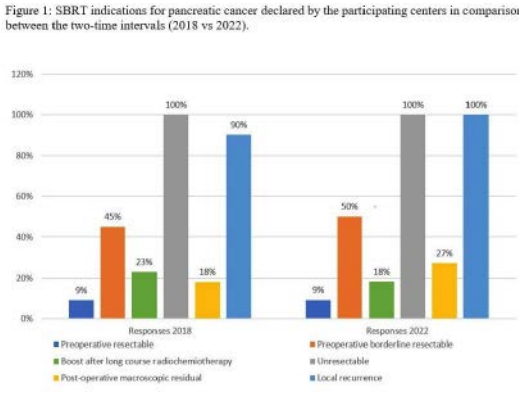

Figure 1.

P025

CONCURRENT EGFR-TKI AND THORACIC RADIOTHERAPY: RETROSPECTIVE EVALUATION OF ACUTE TOXICITY AND POSSIBLE PREDICTORS

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Aim: This retrospective study aimed to evaluate pulmonary toxicity in patients receiving epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKI), in combination with pulmonary stereotactic radiotherapy (SBRT).

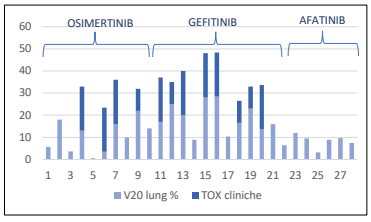
Tables 1 and 2. Graphic 1.

PATIENTS' CHARACTERISTICS		
N° patient		28
Age mean		68 (47-82)
Sex		Men 7 (25%)
		Woman 21 (75%)
Smoker		7 (25%)
Metastatic at diagnosis		19 (67.9%)
CHARACTERISTICS OF THE TREATMENT		
Surgery to primary site		8 (28.5 %)
Adjuvant treatment		2 (7%)
Concomitant TKI		
	Gefitinib	10 (35.7%)
	Afatinib	7 (25%)
	Osimertinib	11 (39.3%)
N lesion		36
DOSE	**FR**	**N°**
50	5	16 (44%)
60	8	9 (25%)
48	4	4 (11%)
Other	-	7 (20%)
Volum PTV (mean)		54 (2.5-234 cc)
V5 lung		31 (6-55)
V20 lung		12 (0.6-28.4)
Dmean lung		7.1 (1.9-13)

TABLE 1 -

CLINICAL ACUTE TOXICITY	GRADE	N
Cough	G1	3 (11%)
	G2	1 (3.5%)
Dyspnea	G1	2 (7%)
	G2	2 (7%)
Chest pain	G1	3 (11%)
	G2	1 (3.5%)
Asthenia	G1	2 (7%)
	G2	2 (7%)

TABLE 2 -



***GRAPHIC 1** - The ordinates represent the values of V20 and the respective clinical toxicity; patients with abscissa from 1-28 treated with the respective EGFR-TKI*

Methods: We identified patients with NSCLC stage IV EGFR-mutant candidate to thoracic SBRT for oligo-progression during EGFR-TKI treatment. Post-treatment CT scans and clinical evaluation were used for the follow-up. A correlation analysis was implemented to evaluate the clinical and radiological acute toxicity through common terminology criteria for adverse events (CTCAE v5.0).

Results: From 2015 to 2021, 28 patients received SBRT in oligo-progression setting during EGFR-TKI treatment (35.7% Gefitinib, 25% Afatinib, 39.3% Osimertinib). Patients' and treatments' characteristics are summarized in Table 1. Acute pulmonary radiological toxicities G1 and G3 (bilateral pneumonia) were reported for 49% and 7% respectively. There were no significant correlations either with patients' features, dosimetric data or TKI therapy. Acute systemic clinical toxicities G1 and G2 were reported for 32% and 21% respectively. Most frequently reported as: dyspnea, chest pain, asthenia and cough; are summarized in Table 2. We identified the pearson correlation coefficient between toxicities ≥ G2 and all of the following parameters: V20 lung (r=0.50), Dmean lung ipsilateral (r=0.46) and therapy with Gefitinib (r=0.40). Afatinib and Osimertinib were not significantly associated with increased toxicity.

Conclusion: Concomitant lung SBRT and EGFR-TKI is safe, with low and manageable toxicity. Prospective studies are requested to confirm these findings.

P026

RUOLO STRATEGICO DELLA RADIOTERAPIA NELL'ERA DELLE CAR-T CELL

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Aims: Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy (tp) is an effective option for the treatment of relapsed/refractory non-Hodgkin B lymphoma. Evidences have emerged of a synergy between radiotherapy (RT) and CAR T-cell tp, and several studies have shown multiple potential roles of radiation in improving CAR-T patients (pts) outcome. RT may be used as a bridge tp for pts with localized chemorefractory disease, or as salvage treatment for pts with localized residual/relapsed disease after infusion.

Methods: We report a case serie of 10 pts treated in our Institute with RT in the CAR T peri-infusional setting: 1 primary mediastinal lymphoma, and 9 diffuse large B-cell lymphoma. 8 pts received tisagenlecleucel (tisa-cel), 2 received axicabtagene-ciloleucel (axi-cel). We used RT as bridging regimen for 8 pts. The RT dose

was 30 Gy in 15 fractions (fr). The site was mediastinum (1 pt), abdominal adenopathy (4 pts), inguinal adenopathy (1 pt), and laterocervical adenopathy (2 pts). Median volume of irradiation was 280 ml (min 79,6 ml, max 635 ml). We also used RT as salvage treatment for localized disease relapse 3 months after infusion in 2 cases. The RT dose was 30 Gy in 15fr on inguinal adenopathy in one pt (volume of irradiation 129.5ml), and 30Gy in 10fr on mediastinal adenopathy in the other one (volume of RT 29.1 ml).

Results: Local response to bridging RT was achieved in all pts. 2 pts had a complete responses, 5 had a partial local responses and 1 a stable disease. Among the 5 pts with partial local response after RT, 4 showed distant disease progression: after CAR-T infusion, a complete disease remission has been obtained in 2 of them. Response to salvage RT was a complete remission in both 2 pts, and one of them underwent consolidation with allogeneic stem cell transplantation. Toxicity was manageable both in bridging and salvage RT. After CAR-T infusion, 3 pts had CRS grade 2, but no one had CRS grade 3-4; only one pt receiving axi-cel had ICANS grade 4 with admission at ICU, but a complete resolution has been obtained after treatment with high dose steroids. At the time of writing, the outcome is favorable in 7 infused pts, and 6 of them are still in complete remission. The remaining 3 pts died for subsequent disease progression.

Conclusions: We showed that RT is feasible and well tolerated as bridging or salvage tp, and it could offer enhanced tumor control for localized residual disease in the peri-infusional setting of CAR-T pts.

P027

COMBINATION TREATMENT WITH PRECISION THERAPY AND SRS: PRELIMINARY RESULTS IN PATIENTS WITH BRAIN OLIGOMETASTATIC NON SMALL CELL LUNG CANCER (NSCLC)

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Aims: To assess feasibility of concomitant SRS with target therapy and immunological drugs in brain oligometastatic non small cell lung cancer (B-NSLC) patients.

Methods: We retrospectively reviewed synchronous and metachronous B-NSLC patients. Inclusion criteria were: oligometastatic disease, proven histology, ECOG performance status [PS] ≤ 2; life expectancy > 6 months and control of the extracranial disease. Oligoprogressive B-NSLC were excluded. Data on the molecular state and PDL-1 expression were collected and patients were stratified into two categories based on the systemic therapy (Tyrosine-Kinase inhibitor, TKI or anti Programmed Death Ligand-1, PDL-1). All patients performed brain Magnetic Resonance Imaging (b-MRI) before being to underwent SRS with Robotic arm LinAc. Progression free survival (PFS) and overall survival (OS)were evaluated. A post SRS b-MRI was obtained to evaluate response defined as complete response (CR), partial response (PR), stable disease (SD), progression (PD) according to RANO -BM (Response assessment in neuro-oncology brain metastases) criteria and radionecrosis (RN) Radiation Therapy Oncology Group (RTOG) CNS toxicity criteria.

Results: 19 patients (median age 69 years) with 37 lesions were evaluated between January 2018 and December 2021. Of them, 9 had a stage IV at diagnosis; only one patient showed ALK mutation, 6 had EGFR mutation and 12 had PDL1 high expression. Immunotherapy (IT) and TKI was administered in 12 and 7 patients respectively. The most frequently treated brain regions were parietal and frontal. All patients received SRS with median dose delivered of 20 Gy in 1 fraction (range 15-25Gy) at a median isodose line of 80% (range 72-80) in 1-5 fractions. Post SRS, among patients treated with IT 8 (66.6 %) reported CR, 2 SD (16,6%), 1 (8.3%) showed appearance of new lesions. 1 (8.3%) showed an increase of treated target after one year ; evaluation in TKI group showed 1 patient with CR (14,28%), 6 PD (85,71%) and no SD. IT group showed median OS and PFS of 41 and 32 months; for TKI group median OS and PFS was 41 and 24 months respectively. No event was classified as a G3-G4 adverse events; 3(25%) patients after IT plus SRS developed RN.

Conclusions: Our preliminary results seem to demonstrate that combination treatment with target therapy and immunological drugs and SRS are safe, effective, and well-tolerated with promising results in IT group. RN remains a critical issue.

P028

CYCLIN-DEPENDENT KINASE4/6 INHIBITOR AND STEREOTACTIC RADIATION IN THE TREATMENT OF HORMONE RECEPTOR POSITIVE BREAST CANCER BRAIN METASTASES

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Aims: Cyclin-dependent kinase (CDK) 4/6 inhibitors are utilized in the setting of advanced, hormone receptor (HR+) positive breast cancer. A potential synergy between radiation therapy (RT) and CDK4/6 inhibitors (CDKi) emerged from preclincial data. We assessed clinical outcomes of patients treated at our institution with the use of CDKi and stereotactic radiation (SRT) in the management of HR+ breast brain metastases.

Methods: We conducted a retrospective analysis of patients who received stereotactic radiotherapy for HR+ brain metastases within 6 months of CDKi administration. The primary endpoint was neurotoxicity during or after stereotactic radiation. Secondary endpoints were local control, brain control, distant control.

Results: It was evaluated a total of 24 lesions treated with stereotactic radiation in 10 patients. Four patients received palbociclib (40%) and 6 patients ribociclib (60%). RT was delivered concurrently in 7 lesions (30%) and sequentially in17 lesions (70%). Median follow-up following stereotactic radiation was 11 months. One lesion (4%) developed radionecrosis without clincal symptoms. None of the patients developed acute severe toxicity. At 6 month 80% of patients presented brain control an 90% of patients distal control. At 12 month 30% of patients presented brain and distal control. None of the patients developed relapse in the treatment site.

Conclusions: Stereotactic radiation to breast brain metastases was well tolerated alongside CDK4/6 inhibitors. Compared to historical data, brain metastases control rates are similar.

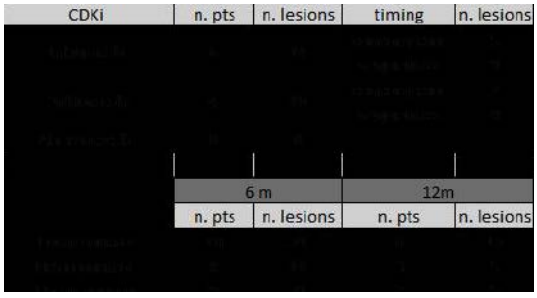

Figure 1.

P029

INTEGRATED STRATEGIES IN LOCALLY ADVANCED PANCREATIC CANCER: PROSPECTIVE STUDY

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Aims: The aim of this study was to evaluate the safety and efficacy of induction treatments in patients with borderline resectable or unresectable locally advanced pancreatic cancer and the efficacy of pre-treatment staging with PET-CT and laparoscopy in addition to CT scan.

Methods: From 2015 to 2022 we evaluated 51 patients with borderline resectable or unresectable pancreatic cancer. A pre-treatment staging was performed with CT scan, 18FDG PET-CT scan and laparoscopy. Patients with metastatic disease were excluded. Suitable patients received induction treatments with FOLFIRINOX, after 4 cycles patients were restaged with CT scan and 18-FDG PET-CT. Patients without evidence of metastatic disease started radiochemotherapy with weekly gemcitabine. After radiochemotherapy, before surgery evaluation, patients performed CT scan and 18-FDG PET-CT scan.

Results: Twenty patients (40%) were excluded from the protocol because of the evidence of metastatic disease, and thus a total of thirty patients were consequently enrolled. Four patients (8%) had a progression of disease after induction chemotherapy. Median follow-up was 12.6 months. Twenty-six patients (52%) completed radiochemotherapy. Seven patients (14%) had a progression of disease after radiochemotherapy. One patient are currently treating. Thirteen patients underwent surgical radical resection (26%). The Median OS and the Median PFS in patients who have completed radiochemotherapy were 15.7 months and 13 months respectively. One-year OS, one-year PFS, one-year LPFS and one-year MPFS were 87.1%, 58.6%, 89.2% and 60% respectively. Patients who underwent resection had a significant longer median OS compared with non resected patients (17 months *vs* 13.2 months, $p<0.05$). The median PFS for resected patients was 14.5 months compared with 8.1 months for non resected patients ($p=0.07$). For the entire cohort of patients the treatment was well tolerated. Only haematological grade 3-4 toxicities were observed.

Conclusions: Altough the follow-up time is limited, these preliminary data of the protocol treatment show promising results for patients with borderline resectable and unresectable pancreatic cancer. The best results were observed in patients who were resectable after the end of study protocol. The enrollment is actually ongoing. Continued optimization in multimodality therapy and an accurate patient selection are crucial for the appropriate treatment of patients.

P030

INTEGRATED INTENSIFIED TREATMENT OF RECTAL CANCER IN THE SETTING OF TOTAL NEOADJUVANT THERAPY (TNT)

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Aims: Total neoadjuvant therapy (TNT) for locally advanced rectal cancer (LARC) is a novel multimodal approach which consists in delivering both induction chemotherapy (CT) and concomitant chemoradiotherapy (CT-RT) prior to surgery in the aim to reduce tumour stage and occult micro-metastases, and consequently favouriting radical surgery. To date, at University of Catania 38 patients have been treated from 2014 to 2022 with TNT approach, with different CT schemes and radiotherapy (RT) schedules. Our aim is to evaluate patients' tolerance to neoadjuvant treatments and the radiological and pathological response after TNT.

Tables 1-2-3.

Table 1

Characteristics		N. of patients	Percentage
Sex	Males	28	73.68%
	Females	10	26.31%
Age	<65 y.o.	6	15.78%
	55-64 y.o.	10	26.31%
	65-74 y.o.	6	15.78%
	>75 y.o.	16	42.10%
Performance Status	100%	16	42.10%
	90%	14	36.84%
	80%	6	15.78%
	70%	2	5.26%
Comorbidities	None	12	31.57%
	Diabetes	8	21.06%
	Hypertension	20	52.63%
	Hypercholesterolemia	6	15.78%
Onset symptoms	Rectorrhagia	16	42.10%
	Irregular alvus	15	39.47%
	Tenesmus	10	26.31%
	Subocclusion/obstruction	7	18.42%
Onset CEA	< 5 ng/mL	16	42.10%
	5.1-5 ng/mL	4	10.52%
	5.1-10 ng/mL	14	42.10%
	>10 ng/mL	2	5.26%
Rectal exploration	Mobile mass	10	26.31%
	Ipomobile mass	24	63.15%
	Immobile mass	4	10.52%
Distance from A.V.	< 5 cm	10	26.31%
	5.1-10 cm	24	63.15%
	> 10 cm	4	10.52%
Stage	T2 N1-2	6	15.78%
	T3 N0	4	10.52%
	T3 N1-2	28	73.68%

Table 2

Total neoadjuvant therapy			N. of patients	Percentage
Chemotherapy schemes	Induction	FOLFOX 3 cycles	16	42.10%
		FOLFOX 4 cycles	12	31.57%
		5-FU 3 cycles	3	7.89%
		5-FU 4 cycles	2	5.26%
		Capecitabine	5	13.15%
	Induction and consolidation	FOLFOX 3+3 cycles	12	31.57%
		5-FU 3+3 cycles	6	15.78%
Radiotherapy schedules	CRRT	180-4800 cGy	12	31.57%
		200-4800 cGy	12	31.57%
	CRRT + Boost	180-900 cGy	12	31.57%
		200-1200 cGy	8	21.06%
	HRT	225-4500 cGy	10	26.31%
		250-5000 cGy	4	10.52%

Table 3

Toxicity (CTCAE v4.0)	Radiotherapy induced		Chemotherapy induced	
	Grade I	Grade II	Grade I	Grade II
Diarrhea	18.42%	15.78%	10.52%	5.26%
Proctitis	21.06%	10.52%	-	-
Dysuria	26.31%	15.78%	-	-
Skin toxicity	21.05%	21.05%	-	-
Hematological toxicity	-	-	7.89%	7.89%
AST and ALT increased	-	-	5.26%	10.52%

Method: From 2014 to 2022, at University of Catania 38 patients affected by LARC have been enrolled (Table 1); all patients performed induction CT (with or without consolidation) with FOLFOX, 5-Fluorouracil infusion or capecitabine. Then, all patients performed concomitant RT-CT together with daily continuous infusion of 5-FU, to a total median dose of 50 Gy, with conventionally fractionated radiotherapy (CFRT) or moderated hypo fractionated radiotherapy (HRT) (Table 2). All patients performed surgery 8-12 weeks after the end of RT-CT treatment. To evaluate the radiological response rate, all patients underwent pelvic MRI with gadolinium and brain-chest-abdomen CT scan both before starting CT-RT and 6-7 weeks after TNT. Then, toxicities during induction CT and concomitant CT-RT and the pathological response after surgery have been evaluated.

Results: After CT-RT all patients underwent MRI restaging: according to RECIST criteria, 28 patients had partial response (PR) while 10 patients had stable disease (SD), no one had progressive disease (PD). About pathological response, actually 20 patients had PR, 8 patients had SD while 10 patients had complete response (CR) with ypT0N0. No one got residual tumour. According to CTCAE v4.0, during induction CT 6 patients had G1-2 G.E. and haematological toxicities, while during CT-RT, 26 patients had G1-2 G.E. toxicity, 16 patients had G1-G2 G.U. toxicity and 16 patients had G1-G2 cutaneous toxicity (Table 3).

Conclusions: Even if more studies are needed to decide the best CT scheme or RT schedule for each patient, to date TNT is considered both a feasible and well tolerated neoadjuvant approach. Moreover, it allows to obtain a good local disease control with an acceptable pathological response rate.

P031

STEREOTACTIC RADIATION THERAPY PLUS PEMBROLIZUMAB FOR PLEOMORPHIC PANCOAST CANCER IN SYNTOMATIC PATIENT

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Aims: Pulmonary pleomorphic carcinoma is a malignant rare subtype of non-small cell lung cancer (NSCLC), with a poor prognosis and no standard treatments have been established. Despite some case-reports of a good response to immune-checkpoint inhibitor, no report of stereotactic body radiation therapy (SBRT) and its association with Pembrolizumab as first-line treatment exists. Also, the treatment of a Pancoast lung cancer may differ from that of other types of NSCLC: its position and close proximity to vital structures make surgery difficult. We herein report the successful treatment of a patient with a pleomorphic Pancoast cancer associating of SBRT

and Pembrolizumab.

Method: We report the case of a 64-year-old male with a left lung mass of the apex (maximum diameters 55x54x50 mm) infiltrating the first two ribs. The patient complained of functional impotence of the left upper limb, drooping eyelid and intense pain (NRS 10), poorly responsive to medical therapy. He was diagnosed with pleomorphic lung cancer by biopsy. The tumor cells showed high PD-L1 expression > 50%. Clinical stage evaluation using contrast-enhanced chest CT and 18F-FDG PET-CT revealed a Stage IIIA (cT3cN1cM0). One week after the first dose of Pembrolizumab (200 mg/body, every 3 weeks), he started SBRT with a dose prescription of 8Gy x 5fx on lesion and nearest lymphnodes plus 3mm-margin for PTV. CTV was measured on simulation CT, on first CBCT and on chest CT performed 45 days after SBRT.

Results: Pain reduction was recorded from 5 days after SBRT. To date, the patient complained slight deficiency of hand strength and ulnar paresthesias, with episodic mild-intensity pain (NRS 5). Response assessment after 3 cycles of Pembrolizumab revealed marked reduction (-50,7 %) in tumor diameter, without pulmonary fibrosis of surrounding parenchyma. CTV was 271.3 cc, 302.8 cc and 149.2 cc on simulation CT, at the start of SBRT and at first follow up, respectively (Figure 1).

Conclusions: To our knowledge, this is the first study in literature about the use of SBRT plus Pembrolizumab as first-line therapy against pleomorphic Pancoast cancer. This kind of association appears beneficial in symptomatic patients. It is also effective, at least when PD-L1 expression is high, probably due to high equivalent doses of SBRT and synergic immune system stimulation related to circulating antigens from SBRT and to immunotherapy. Further studies with a larger number of patients and longer follow-up are needed.

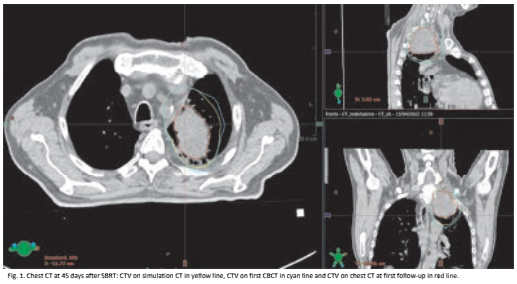

Fig. 1. Chest CT at 45 days after SBRT: CTV on simulation CT in yellow line, CTV on first CBCT in cyan line and CTV on chest CT at first follow-up in red line.

Figure 1.

P032

HYPERTHERMIA IN ASSOCIATION WITH RADIOTHERAPY AND CHEMOTHERAPY FOR SOFT TISSUE SARCOMAS OF TRUNK AND LIMBS

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Aim: The aim of the study is to analyze toxicity and efficacy of addition of HyperThermia (HT) to both radiotherapy (RT) and chemotherapy (CT) in patients affected by Soft Tissue Sarcomas (STS) localized to the trunk and limbs.

Methods: We retrospectively investigated 18 patients (7 males and 11 females all with Performance Status ECOG 0-1, age 43-87 mean 63.6) affected by STS treated with HT combined with RT and/or CT. HT session was performed immediately after RT and within three hours from the administration of chemotherapy. Duration of each HT session varied from 70 to 90 minutes to guaranteethat target temperature was greater than 40 ° for at least 60 minutes. BSD-500 or BSD-2000 system were used depending on depth of lesion.

Results: The most represented histology was pleomorphic undifferentiated sarcoma. 16 patients had stage III A/B disease (according to AJCC Cancer Staging Manual. 8th edition) and 2stage IV for concomitant lung metastases. In 7 patients the lesion treated was the primary tumor and in 11 a relapse of the disease. The mean target size was 9.1 cm (range 1-20 cm). HT was associated to RT in 9 patients, to radiochemotherapy (gemcitabine-based) in 3 patients, to CT in 1 patient. 5 patients underwent CT (anthracycline and ifofosfamide) following with RT and HT. In 13 patients, the intent of treatment was neoadjuvant, in 2 postoperative after incomplete resection and in 3 cases for unresectable disease. Mean radiation dose was 52 Gy (range 48-60 Gy). 16 patients were treated with superficial HT and 2 with deep HT. No skin toxicity greater than grade 2 was detected and only one patient had hematological toxicity greater than grade 3. Among 13 patients treated with neoadjuvant purpose 9 underwent surgery and 2 are going to be evaluated for surgery. In all 9 cases R0 resection was obtained and in 4 cases a complete pathological response was reported. With a median follow-up of 17.1 months, 5/18 (27.7%) patients had a progression of disease, 3 a distant progression (2 lung and 1 lung and abdomen) and 2 local progression (in 1 case out filed recurrence in the other case patient was treated without RT). Overall, the local control rate was 89.9%.

Conclusions: In our experience, the integration between HT, radiotherapy and chemotherapy in patients affected by STS of trunk and extremities was feasible

achieving a good local control. However, a larger number of patients and a long follow-up are needed to better estimate features of integration of HT radiotherapy and chemotherapy.

P033

1.5T MR-GUIDED DAILY ADAPTIVE RADIOTHERAPY: PRELIMINARY CLINICAL REPORT OF THE FIRST 5000 FRACTIONS DELIVERED AT ADVANCED RADIATION ONCOLOGY DEPARTMENT (ARO) IN NEGRAR (VR, ITALY)

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Aims: 1.5T MR-linac improves target volume and adjacent OARs visualization, ensuring high precision in radiation treatment delivery. Daily MR-imaging allows on-table adapted planning and real-time intra-fraction imaging without additional exposure to radiation. Our department implemented the first high field MRgRT system in Italy and herein we present the preliminary report of the first 5000 fractions delivered. We aim to describe the clinical implementation, feasibility, toxicity and patient tolerability of daily adapted RT.

Matherial and Methods: Since October 2019, Elekta Unity MR-linac has been available in our department. A prospective observational study for the clinical use of Elekta Unity is currently ongoing in our department: patients affected by prostate adenocarcinoma, pancreatic cancer, oligometastases and patients requiring retreatments were included. Two different workflow were used depending on the OARs daily anatomy: Adapt To Position (ATP) where the reference plan position is adjusted rigidly to match the position of the targets and OARs, and Adapt To Shape (ATS) where a new plan is created to better match the anatomy of the day. Toxicity and quality of life were assessed at baseline and after treatment using the CTCAE v5.0. Patient-reported outcomes of prostate cancer patients were investigated by means IPSS, ICIQ-SF, IIEF-5, EPIC-26, EORTC-QLQ-C30 and PR-25 questionnaires.

Results: Between October 2019 and June 2022, 590 patients with 675 target sites were treated with MR-guided radiation therapy in 5000 total fractions. Median patient age was 70 years (39–86). Among 675 tumor sites, the most frequently treated region was pelvis (n=549, 81%). The most common diagnosis was prostate cancer (n=326). On–table adaptive radiation therapy was used at every treatment session: ATP workflow in 63 fractions (1%) and ATS workflow in 4937 fractions (99%), respectively. Median prescribed dose was 35 Gy (20–67.5 Gy) in median 5 fractions (5–30). Mean total treatment time was 43 minutes (20–56). Treatments were well-tolerated and no acute G>3 toxicities were reported. Concerning the PROMS, all questionnaires showed no relevant deterioration between the pre-, post-RT and follow-up evaluations.

Conclusions: MR-guided radiation treatment using 1.5T MR-linac has been successfully implemented into clinical routine at our department. The data reported support an optimal profile of tolerability of daily on-table adaptive radiation therapy in acceptable time slots. These results are confirmed by PROMs.

P034

RECONFIGURING MULTIDISCIPLINARY TEAM DISCUSSIONS: IDEATION AND DEVELOPMENT OF A SPECIFIC PLATFORM FOR PRESENTATION, COLLEGIAL DISCUSSION AND RECORD OF CLINICAL CASES

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Aims: In the era of Covid - 19 pandemic, taking into account also the increasing need for respect of patients' privacy, we tried to identify a system that could allow specialists from different centers to take part in multidisciplinary discussions in a safe and performing setting.

Methods: We analyzed the number of clinical cases discussed annually in our center within the various multidisciplinary teams dedicated to different tumour types. We identified the two groups with the highest number of cases discussed: the thoracic cancer group (average of 875 cases discussed per year), and the breast cancer group (average of 1650 cases discussed annually). The specialists taking part in these discussions then meet in a series of Delphi Rounds, in order to identify the basic needs of each multidisciplinary group. Three requirements were identified as essential above all the others: the possibility of easily accessing discussions even remotely, of effectively sharing the details of clinical cases and of accessing the results of the discussion in a safe and respectful of the patient's privacy way. With the assistance of a specialized company that provided us with adequate IT support, we therefore designed a web - app that would respond to the needs of the multidisciplinary groups themselves.

Results: The platform we have developed allows specialists from different centers to take part in the meetings by connecting remotely, to upload a dedicated form filled with the clinical details and all the documents that may be important (e.i. imaging, histological examinations, various reports, etc). Once the case has been discussed, the collective decision is recorded in the app, which then creates a report for each individual clinical case and also a letter for the patient, reporting the outcome of the mee-

ting. All the documents remain available to every specialist, who can retrieve them by accessing the platform via browser, thus avoiding the need to exchange sensitive data via email. In February 2022 the web app has become operational, and currently two multidisciplinary teams of our center, thoracic cancer and breast cancer groups, have started to use it successfully.

Conclusions: The use of a specific platform for multidisciplinary meetings has proved to be a winning strategy, which allows specialists from different areas to interact effectively, without neglecting the aspect of the correct and appropriate management of the clinical data of each individual patient.

P035

EARLY DETECTION OF SKIN TOXICITIES IN BREAST CANCER PATIENTS UNDERGOING RADIOTHERAPY USING AN APP-CONTROLLED MONITORING INTERVENTION

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Aims: Breast cancer patients treated by surgery and undergoing radiation therapy may often experience clinically significant skin toxicity, adversely affecting cosmesis, quality of life, and treatment compliance. Usually, the Patient's clinical condition is recorded during scheduled, time-limited office visits and patients might forget to discuss symptoms that occurred days before. The goal of our study is to introduce a new operating model for continuous tutoring and assistance in the context of Patient-Reported Experience Measures (PREMs) and Patient-Reported Outcome Measures (PROMs) through the use of a dedicated application (app) during radiation treatment and follow-up period.

Method: We performed a literature review on the main databases to build up a proper questionnaire to propose to the patients to detect early skin toxicity. The questions were uploaded to our app, which can collect data from patients and make it available to an Electronic Data Capture (EDC) at its disposal for further statistical evaluations in the middle and at the end of the treatment period. It is possible to upload a picture of the Patient's breast.

Results: We developed our questionnaire based on validated scores. The Patient must answer the questionnaire at different "assessment points": the first access to the app, once a week, beginning from the end of the first week, once a week for the first three months of follow-up. At each evaluation point, the Patient answers the questionnaire through the app and uploads a picture of her breast. The machine learning-assisted analysis of these data will allow identifying patients profile that may be used as risk categories for the early diagnosis of skin toxicity.

Conclusions: Our tool may help patients, caregivers, and physicians to improve the quality of the treatment by putting in the very center the active role of the Patient himself. The subsequent phase of our study will require testing our developed app with patients to validate it fully. Assessing early side effects will lead to quicker response and thus lower inconvenience for patients, optimizing assistance and follow-up practices, and obtaining a better outcome.

P036

RADIOSURGERY AND REGORAFENIB IN RECURRENT HIGH-GRADE GLIOMAS: IS IT FEASIBLE?

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Purpose: In recurrent glioblastoma (GB) no standard therapeutic approach is reported, so surgery, chemotherapy and reirradiation could be proposed. Recently Regorafenib was approved for recurrent GB. The present retrospective study was conducted to evaluate safety and efficacy of re-irradiation with radiosurgery o stereotactic radiotherapy (SRS/SFRT) in patients with recurrent GBM in association to Regorafenib.

Material/Methods: Inclusion criteria were as follow: histological diagnosis of GB; carrying out primary/adjuvant chemo-radiotherapy treatment; magnetic resonance imaging (MRI) evidence of recurrent disease according to Response Assessment in Neuro-Oncology (RANO) criteria after primary/adjuvant treatment; good performance status. All patients underwent re-RT with SRS/SFRT with a median dose of 24 Gy (range 18-36 Gy) and median fractions of 5 (range 1-6), Clinical outcome was evaluated by neurological examination and brain MRI performed, 1 month after radiation therapy and then every 3 months.

Results: From November 2019 to December 2021, 16 patients (6 women and 10 men) affected by GB recurrence were treated by re-RT plus Regorafenib. The median time occurred between primary/adjuvant RT and disease recurrence was 8 months (range 2-20). Moreover, in 6 cases (40%) a second surgery was performed and in other

6 cases a third RT was administered. At the time of the analysis, 11 patients were dead for disease. The median OS and PFS after recurrence were 8 and 6 months. Regarding SRS/SFRT toxicity no acute or late neurological side effect grade ≥ 2 were reported. No case of radionecrosis was detected. One patient that received Regorafenib after 45 days from re-surgery, suffered by surgical wound dehiscence, requiring the chemotherapy interruption. Grade 3-4 hematologic toxicity occurred in 5 cases, asthenia occurred in all patients.

Conclusion: re-RT with SRT/SFRT in association with Regorafenib is a safe and feasible treatment and a combined ones as a better option for selected patients.

P037

RADIATION THERAPY IN PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICE (CIED): A PRELIMINARY ANALYSIS OF RADIATION EFFECTS ON 42 PATIENTS

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Aims: In the last years the number of patients with a Cardiac Implantable Electronic Device (CIED) undergoing Radiotherapy (RT) has exponentially increased. During RT different kinds of damage to the device can occur. In our Department, since 2017, we adopted a protocol based on Literature data to reduce the risk of devices damages. Here we describe our approach and present the related results.

Method: We retrospectively reviewed the records of 42 patients with a pacemaker (PM) or an Implantable Cardioverter Defibrillator (ICD). After treatment planning, doses to device are evaluated, then patients perform a cardiological check and are stratified into 3 risk classes: low, moderate, high. Risk probability is based on: type of device (PM or ICD), patient characteristics (PM-dependency, risk of arrhythmias), RT treatment planning (beam type and energy, site of treatment, CIED doses). The cumulative dose (Dmax) to CIED can be considered low if <2 Gy, moderate = 2-20 Gy, high >20 Gy. According to patients risk stratification, Cardiologist suggests the appropriate procedure to follow that can include: device adjustment (relocation or reprogramming), use of proper equipment (audiovisual monitor, magnet, ECG, pulse oximeter), presence of specific staff (electrophysiologist, nurse, technician, anesthesiologist). Scheduled cardiological evaluations are performed in the middle and at the end of RT.

Results: We evaluated 34 treatments with beam energy ≤6 MV. 29 patients had a PM and 5 an ICD all implanted in the subcutaneous tissue of the left supraclavicular fossa; 5 were device-dependent. 59% patients resulted as low risk, 26% moderate, 15% high. 9 patients did not receive any dose to the device, 4 received a Dmax>20 Gy. The maximum dose delivered to the device was 52,7 Gy. No case of relocation or reprogramming occurred. In 1 case, despite being indicated, regional nodal irradiation was omitted to exclude the device from the radiation field. No device malfunction was reported. 17 patients had a follow-up longer than one year and 12 of them are still undergoing follow-up. 17 patients died for progression of disease or other causes.

Conclusions: These are the preliminary results of our analysis. In our experience and according to Literature, although few clinical data have been evaluated, RT in patients with CIED seems safe especially with beam energy ≤6 MV. Collaboration between various specialists is extremely important to manage these patients appropriately.

P038

PHASE II TRIAL OF LINAC-BASED STEREOTACTIC ARRHYTHMIA RADIOABLATION (STAR) FOR PAROXYSMAL ATRIAL FIBRILLATION IN ELDERLY: PLANNING AND DOSIMETRIC POINT OF VIEW

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Aim: A prospective phase II trial evaluating LINAC-based stereotactic arrhythmia radioablation (STAR) safety in elderly population started in 2021. Here, dosimetric and planning data were reported.

Methods: A vac-lock bag was used for patients' immobilization in the supine position and a Computed Tomography was performed. The clinical target volume (CTV) was identified by radiation oncologist and cardiologist and was defined as the area around pulmonary veins. An internal target volume (ITV) was added to CTV to compensate heart and respiratory movement. The planning target volume (PTV) was defined adding 0-3mm to the ITV. STAR was performed in free-breathing with a PTV prescription total dose (Dp) of 25Gy/1 fraction. A "simultaneous integrated protection" dose distribution was created at the interface between PTV and organs at risk in order to ensure the tolerability of critical structures. Flattening Filter Free Volumetric Modulated Arc Therapy (VMAT) plans were generated, optimized and

delivered by TrueBeamTM (Varian Medical System). Image-guided radiotherapy with Cone Beam CT and Surface-Guided RadioTherapy with Align-RT (Vision RT) were employed.

Results: From May 2021 to March 2022, 10 elderly patients were treated. Mean CTVs, ITVs and PTVs were 23.6 cc, 44.32 cc, 62.9 cc respectively; while the mean prescription isodose level and D2% were 76.5% and 31.2Gy, respectively. Regarding organ at risk, average heart and left anterior descending artery (LAD) Dmean were 3.9 and 6.3Gy, respectively; while mean Dmax for LAD, spinal cord, left and right bronchus and esophagus were 11.2, 7.5, 14.3, 12.4 and 13.6Gy respectively. In terms of 4D-CT data, only Superior-Inferior movements reported an amplitude of 0.6 cm, while for Medio-Lateral and Aanterior-Posterior an amplitude of 0.1 cm was documented The Overall Treatment Time (OTT) was 3minutes.

Conclusion: The reported STAR dosimetric data showed an optimal target coverage, sparing surrounding tissue, in a 3 minute of OTT. Considering the large diffusion of LINAC in the world and the large AF elderly population, the present collected data are interesting, LINAC-based STAR for AF could represent a valid non-invasive alternative for elderly who were excluded from catheter ablation.

P039

IN VIVO COMBINED RADIOTHERAPY AND WHOLE-BODY HYPERTHERMIA ON PANCREATIC CANCER MODELS: IS A SYNERGIC EFFECT POSSIBLE?

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Aims: Pancreatic cancer(PC) has a poor prognosis due to its aggressiveness and ability to metastasize at early stage. Currently, its management remains a challenge because it is resistant to the conventional treatment approaches (Chemo-Radiotherapy). The abundant stromal compartment implicated in the mechanism of hypoxia is the main cause of tumor resistance. Hyperthermia may reduce the hypoxic environment enhancing the radiotherapy effect. On this regard, hyperthermia efficacy has been already validated in the preclinical settings for PC management. Therefore, the establishment of integrated treatments would be a promising strategy for the management of PC. Our aim is to investigate the effect of combined radiotherapy(RT) and hyperthermia(HT) in a chick embryo chorioallantoic membrane (CAM) pancreatic tumor model.

*Methods:*CAM models of PC have been produced through our standard protocols. Fertilized chicken eggs are punctured on EDD3 (embryonic development day 3) and PC cells (3x106 BxPC-3) are inoculated on the CAM at EDD6. The eggs are incubated for 4 days and randomized into six different treatment groups. HT(41.5°C for 6 h) is administered with a customized heating device (ElmediX).

The groups have been divided as follows:

- Two groups received only RT at a dose of 1 Gy or 2 Gy on EDD12 and EDD14.
- Two groups received an identical RT schedule, while HT was administered on EDD10, EDD12 and EDD14.
- Control groups comprised a normothermic condition (37.5°C) and a hyperthermic condition.

The tumor volumes were collected using a portable digital microscope before and after the treatments. On EDD15, the experiment was concluded, and tumors were harvested for following end-point analysis.

Results: From data analysis, tumors treated with RT and HT appear to grow more slowly compared to normothermic or single-treatment controls although the result is not statistically significant.

Conclusions: We found that HT may positively affect RT in CAM tumor model grafted with PC cells. Due to the small sample size, the evidence for a potential advantage of adding HT to RT in PC should be confirmed by further biological analysis. However, the results obtained may suggest that there is a combinatorial effect between RT and HT and this appears to be encouraging given the lack of therapeutic efficiencies in PC. The possibility of translating these results into clinical practice to improve the outcome for patients affected by this malignancy represents the missing piece.

P040

SURFACE GUIDED RADIOTHERAPY (SGRT) IN PATIENT POSITIONING AND IN THE EVALUATION OF SETUP SHIFTS: OUR EXPERIENCE

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To assess if the Surface Guided Radiotherapy (SGRT) improved the positioning of the patients and if it reduced the shifts during the treatments. We collected data on patient's positioning with and without the SGRT. The sample included 10 patients, four breasts, two upper limbs (two right humeri), a thorax (lung), a pelvis (bladder) and two lower limbs (a right and a left femur). The patients were treated with conventional linac using the SGRT system IDENTIFY™ every other day (Varian,

Palo Alto), in order to compare the daily variation of any possible shifts from the setup position. We used the inclined plane and ProStep™ (CIVCO) as immobilization systems. The portal images in MV or CBCT were employed as daily verification. The data show that using the SGRT in breast treatment seems to reduce the shifts in its entirely, with an average shift reduction of 0.19 cm (-82%) in the vertical axis, of 0.21 cm (-63%) in the longitudinal axis and of 0.16 (-106%) on the lateral one (Figure 1). As for the upper limb, the treatment without IDENTIFY seems to be not inferior than the one with the addition of the SGRT. However, the evaluation of the correct position of the limb using SGRT would reduce the shift in the lateral axis, highlighting how the portal verification alone would not allow the evaluation of any proximity or distance of the arm from the body, as well as the intra- or external rotation of the limb. Finally, the use of the SGRT in the treatment of the lower limb, would significantly reduce setup shifts on all axes. The statistical analysis of the data, performed using the Wilcoxon test, showed a statistically significant difference ($p < 0.05$) between the group of patients treated by IDENTIFY and those treated without the SGRT in the treatment of the breast, while no statistically significant difference between the two groups in the other districts treated. The SGRT seems a potentially useful method in patient positioning and in checking any excessive shifts from the setup plan, thus also reducing the treatment time. However, a larger sample is needed to demonstrate a real benefit in terms of reducing the amount of the shifts.

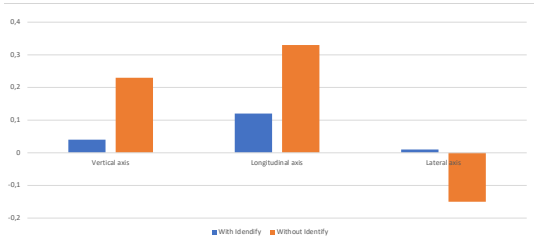

Figure 1.

P041

RADIOFREQUENCY THERMOABLATION AND HYPOFRACTIONATED RADIOTHERAPY COMBINED TREATMENT FOR BONE METASTASES: A RETROSPECTIVE STUDY

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Introduction: Bone metastases (BMs) are the common cause of cancer-related pain, as approximately 45% of cancer patients suffer from bone pain (BP). Radiotherapy (RT) is well established as BP treatment strategy; also, other approaches have been shown to be effective in this setting. Radiofrequency thermoablation (RFA) in a combined strategy with RT appears to be feasible and effective in the treatment of metastatic BP ensuring a better quality of life. Aim of this retrospective study was to describe a case series of patients with painful osteolytic lesions at risk of fracture treated with the RFA-RT combined approach, analyzing local control and pain control as outcomes.

Methods: Data of all patients with BM treated with combined approach in our center from April 2016 to June 2020 were retrospectively analyzed. Patients underwent RFA followed by cementoplasty on the same day and RT in a second phase. RT dose ranged between 30 and 37.5 Gy in 5/10 fractions. BP was evaluated according to the numeric rating scale (NRS), at the beginning of treatment and at 1, 2, 3, 6, 9, and 12 months from the end of combined treatment.

Results: A total of 27 patients were treated from April 2016 to June 2020 with RFA-RT combined approach. The large majority of patients underwent stereotactic body radiotherapy (SBRT) (23/27). All patients experienced an NRS value decrease >2 at 1 month and between the first and second months. NRS mean value reached 0 at 3, 6, 9, and 12 months' evaluations.

Discussion/conclusion: The results of this retrospective analysis of patients treated with RFA-RT combined approach for BP support its safety and efficacy in terms of pain reduction. SBRT role in this combined approach has to be investigated in randomized trials.

P042

POST-OPERATIVE HYPOFRACTIONATED RADIOTHERAPY FOR ELDERLY PATIENTS WITH T1-2 N0 BREAST CANCER TREATED WITH HORMONE THERAPY OR CHEMOTHERAPY: OUTCOME AND TOXICITY IN OUR EXPERIENCE

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Aims: About 30% of breast cancer occur in women aged >70 years although elderly patients are often excluded from both retrospective and randomized trials and treated suboptimally. The aim of this retrospective analysis was to evaluate outcome and toxicity in a group of breast-cancer elderly patients with T1-2 N0 cancer treated with a hypofractionated schedule, with or without systemic therapy and hormone therapy or chemotherapy.

Method: Between June 2005 and December 2020, three hundred fifty-two (352) breast cancer patients >70 years with pT1-2 N0 cancer were treated at Radiotherapy Department in Taranto with a total dose of 42.56 Gy (2.66 Gy/die) without adding a boost. The mean age was 77 years (range: 70-89 years). All patients underwent conservative surgery while axillary dissection or sentinel lymph node biopsy was performed in 85.5% of patients. Pathological stage was pT1 in 48.9% and pT2 in 51.1% of patients. Most of patients (79.5%) with positive estrogen and/or progesterone receptors received hormone therapy while negative-receptor women received adjuvant chemotherapy. Acute and late toxicity were evaluated according to the RTOG/EORTC scale. Local recurrence rate, metastasis rate, overall and disease-free-survival were also calculated.

Results: Local relapse rate was 3.4% with a mean follow-up of 102 months (range: 6-178 months) while only ten patients (2.8%) experienced distant metastases and died (seven with bone metastases, three with lung metastases). The disease-free-survival was 95% at 5 years and the overall survival was 91% at 5 years considering that twenty-two women died for cardiovascular disease or other no-cancer-related reasons. Acute skin toxicity was G1 for 73.3% of patients and G2 for 14.7% of patients while 19.3% of women developed late skin toxicity (G1 for 16.5% of patients and G2 for 2.8% of women). No acute lung toxicity was observed while only three patients had late lung fibrosis.

Conclusions: Postoperative radiotherapy with hypofractionated schedule in woman >70 years old resulted in mild early and late toxicity with excellent local control and survival. This is a convenient treatment option for both older patients and health-care providers.

P043

STEREOTACTIC RADIATION THERAPY AND MENINGIOMAS IN GERIATRIC PATIENTS: OUR EXPERIENCES

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Aims: To evaluate toxicities and local control in geriatric patients with diagnosis of meningioma submitted to radiosurgery and stereotactic fractionated radiotherapy.

Patients and Methods: We retrospectively evaluated all patients with diagnosis of meningioma from July 2007 to May 2022 afferent in our center. Among these, all patients aged >65 have been selected and, subsequently. All patients had a life expectancy >6 months, Charlson Comorbidity Index (CCI) age-weighted with a value ranging from 2 to 8 and Karnofsky Performance Status ≥ 60.

Results: We identified 497 treated with Stereotactic Radiotherapy. 192 lesions were in the convexity, 251 of the skull-base, 51 parasagittal, 3 patients presented spinal lesions. 58.9% and 41.1% of 497 patients were over-65 and over-75, respectively. In 30,2% was delivered a treatment in single fraction, and in 69.8% a fractionated technique has been chosen (49.9% five fractions, 19.9% two, three or four fractions). All patients selected to radiotherapy had an age-weighted CCI> 5. Patients' acute toxicities have been evaluated according to CTCAE v4.0 and the Grade 1 and 2 of the scale will be considered as ordinary adverse events, Grade ≥ 3 toxicities will be defined as severe adverse events. Local Control (LC) is defined as the time from the Stereotactic Radiotherapy to locoregional progression, as measurable tumour lesion increases of more than 25% compared to initial diameters according to the Response Evaluation Criteria in Solid Tumours (RECIST) response criteria. After the treatment, toxicities occurred in 13.7% of 497 patients: particularly 2,1% presented symptomatic edema, 6.1% headache G2, 8.5% dizziness G2. None of the patients showed acute toxicity ≥G3. With a median follow up of 6.7 years, 76%, 19% and 5% cases showed stable disease, partial response and radiological progression, respectively.

Conclusions: Our experience shows that the stereotactic radiotherapy in the geriatric patients with meningioma is feasible and well tolerated with low toxicities profile, without substantially differences between the therapy delivered in single fraction compared to fractionated course.

P044

GLIOBLASTOMA IN ELDERLY PATIENTS: TREATMENTS AND OUTCOMES IN A REAL-LIFE SETTING

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Background: Management of glioblastoma (GBM) in the elderly population is challenging and it is well known that in the near future, more than half of patients with this tumour will be over the age of 65. Unfortunately, GBM is associated with a poor prognosis in the elderly and treatment is still controversial and several questions remain unanswered. This analysis aims to describe the clinical practice in these setting of patients evaluating the impact of prognostic factors and total treatment volume on outcomes in GBM treated with radiotherapy with concomitant and adjuvant chemotherapy

Method: Patients with > 65 years with a histological diagnosis of GBM were considered for this analysis. Patients received standard RT (60 Gy over 6 weeks) or hypofractionated RT (35–40 Gy in 10–15 daily fractions) on tumor bed +/- residual mass + 2 cm. All patients received adjuvant Temozolomide (TMZ): six cycles if disease was absent, or until disease progression or unbearable toxicity in the other cases. A survival analysis was calculated using Kaplan-Meier method.

Results: From January 2016 to December 2021, 149 patients were observed (M/F: 54/92). The compliance to radiation treatment was 98% and three patients received only chemotherapy with TMZ. The median age was 76.5 yrs (range 65-88). Ninety-four patients (63.1%) underwent to standard radiotherapy with a total dose of 60 Gy over 6 weeks. The median number of cycles of adjuvant TMZ was 4 (1-12). Toxicity was haematological and mild, G3 piastrinopenia and neutropenia being observed only in 3 patients. With a median follow-up of 38 months (range 7-90), median progression-free-survival was 7 months, 2-yrs OS was 16%. Median overall survival (OS) was 11 months, 2-yrs OS was 13.7%, no patient being alive at 5 years. A complete surgery vs partial vs biopsy (p=0.0001), the age >80 years (p=0.003), the ECOG 0 vs ECOG >1 (p=0.01), the hypofractionated RT vs standard RT (p<0.0001) and the total treatment volume < or > 400cc (p=0.0007) proved to improve OS. All patients with > 80 years underwent to surgery (70% subtotal) except one patients that received the biopsy and to hypofractionated RT with concomitant TMZ with mild toxicity

Conclusions: Our analysis suggests that radio-chemotherapy is well tolerated also in elderly with an improved OS for higher doses of RT and lower total treatment volumes; age ≥ 65 yrs represents the cut-off to consider the age an unfavourable prognostic factor, that remains independent.

P045

ELDERLY PATIENTS WITH GLIOBLASTOMA: BENEFITS AND EFFICACY OF HYPOFRACTIONATION RADIOTHERAPY PLUS TEMOZOLOMIDE

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Aims: To evaluate Overall survival (OS), Progression Free Survival (PFS) and toxicity in elderly patients with Glioblastoma (GBM) treated by hypofractionated radiotherapy (HFRT) and chemotherapy (CHT) VS standard fractionation plus CHT or only adiuvant RT.

Methods: From November 2018 to December 2021 we retrospectively evaluated all elderly patients (≥ 65 years) with histological diagnosis of GMB, Karnofsky Performance Status (KPF) ≥ 50, and submitted to HFRT +/- Temozolomide (TMZ) 75 mg/mq.

Results: In the period of observation 63 patients with a diagnosis of GBM were treated in our center, of these 23 were over 65 years old, subsequently divided in three groups: HFRT alone, HFRT plus TMZ and STUPP protocol. A median KPF of 70 was observed (range 50-90). The median age was 72 (65 - 81 years). All patients underwent surgery resection before our treatment. To the HFRT alone group (patients unfit to TMZ), 5 patients, a dose of 40.05 Gy/15Fx (2.67 Gy/die) was delivered. HFRT plus TMZ group, 7 patients, received 75mg/mq die concurrent to RT followed by six adjuvant courses 150-200mg/mq. In the STUPP group, 7 patients were treated The 6-12 months median OS were 90% and 20% for the group of HFRT-alone; 100 % and 80% for the group of HFRT+TMZ and, 78% and 50% for the third group treated with 60Gy + TMZ. The median PFS was 7, 9, 8.5 months for the first, second and third group respectively. Treatment was well tolerated in most of patients. Two patients of third group reported thrombocytopenia resulting in temporary TMZ interruption; two patients showed cutaneous toxicities (St. Johnson like syndrome) which disappeared after one week of TMZ interruption. Temporary hair loss was present in 100% of cases, headache and other neurological symptoms in 2, 3 and 5 patients of first, second and third group respectively. Nausea (G1) relieved in 1 patient treated by standard fractionation and TMZ.

Conclusion: HFRT plus Temozolomide seems to be an effective and safety treatment in absence of severe

comorbidities. Our experience confirms over-65 eligibility patients with an OS and PFS comparable to literature data without substantially differences of toxicities in all groups.

P046

RESILIENCE VERSUS FRAILTY IN THE OLDER ADULTS UNDERGOING RADIO-ONCOLOGICAL TREATMENT FOR PROSTATE CANCER

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Frailty is the inability to resist stress and fall into a condition of disability due to the same. Resilience, in its opposite, represents the ability to withstand stress. Each individual undergoing cancer treatment has a different level of resilience. Prostate cancer is characterized by a higher incidence in the older adult population and by the correlation due to treatments with conditions such as osteosarcopenia, metabolic syndrome, and an increase in cardiovascular risk. All states underlie an increased risk of developing frailty.

Aims: This study aims to identify the resilience index in a population of FIT patients undergoing early-stage prostate cancer treatment.

Methods: Patients older than 70 years with a new prostate cancer diagnosis were assessed through a comprehensive geriatric assessment (CGA) and enrolled only if FIT. Performance measures such as SPPB, hand grip test, and total body DEXA were carried out to assess muscle mass and sarcopenia risk. The assessments were repeated quarterly for 12 months.

Results: 70 "FIT" patients with early-stage prostate cancer had to undergo radio-oncological treatment, and ADT was enrolled consecutively. The mean age was 80 years (70-92 years). In most patients, there was a progressive reduction of physical performance measures and muscle mass assessed by DEXA scan with an increase in adipose tissue and a tendency to metabolic syndrome. In particular, a significant reduction in muscle strength was highlighted ($p < 0.001$), with evidence of a picture of pre-frailty condition.

Conclusions: Our study highlighted the possibility of tracing a resilience index for each patient undergoing radio-oncological treatment capable of determining the transition to a state of frailty. This index becomes essential in a supportive care relationship during treatment and the follow-up of these patients.

P047

RECTAL CANCER IN GERIATRIC PATIENTS: EXPERIENCE OF INTEGRATED DEFINITIVE OR NEOADJUVANT RADIO-CHEMOTHERAPY

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Abstract: Neoadjuvant Radiochemotherapy (nRCT) is standard of care in locally advanced rectal cancer (LARC) before surgery. Geriatric pts are rarely fit for such an approach and often a non-surgical treatment is applied. We report our experience on safety and efficacy of a definitive or neoadjuvant CRT in this setting.

Table 1. Patient distribution.

Patient and Tumor Characteristics		
Gender	**Male**	15
	Female	11
Age = Median 81 (Range 75-94)		
TNM Stage	**T3**	18
	T4	8
	N0	6
	N1	13
	N2	5
	NX	2

Methods: Between January 2017 and January 2022, we enrolled 26 pts (age 75-94) with T3-4 N0-2 M0 disease, evaluated using CGA index. Integrated CRT was used in 22 pts, while 4 were treated with exclusive RT, due to cardiovascular comorbidity. Long-course radiotherapy with different techniques was applied in all pts, with conventional or moderate hypofractionated schedules, to a total dose of 45-62 Gy. Fluoropyrimidine monotherapy was used in all cases, while 10 pts were treated with an oxaliplatin intensification. Fourteen pts underwent surgery.

Results: After median follow-up of 26 months (range 3-46), 22 pts showed single or multiple G1-2 CTCAE v6.0 toxicity (16 GI, 13 GU, 8 haematological, 12 cutaneous, while only 3 had G3 GI toxicity. A partial response was seen in 13 patients, 10 had a stable disease, 3 had complete response. Median duration of local control was 26 months in pts treated with definitive CRT, while it was longer among pts underwent surgery. Three pts had local relapse and require further treatments.

Conclusion: Neoadjuvant or definitive CRT is feasible and safe even in the majority of elderly patients. Treatment allows a good disease control for an adequate period of time. Further studies are needed to standardize combined treatments in this population.

Table 2. Treatment details.

Chemotherapy	
Induction	
Folfox	10
5-FU	11
None	5
Concomitant	
5-FU	22
None	4
Adjuvant	
Folfox	8
5-FU	8
None	10
Radiotherapy	
Conventional (45Gy/25 fr)	4
Conventional hypofractionated - *(50gy/25 Fr)* - *(46 Gy/23 Fr)*	 8 2
Moderate hypofractionated - *(50 Gy/20 Fr)* - *(45 Gy/20 Fr)* - *(55 Gy/22 Fr)*	 5 6 1
Boost - 9 Gy/5 Fr - 10 Gy/5 Fr - 12 Gy/ 6 Fr	 4 2 2

P048

IS THERE AGE DISCRIMINATION IN RADIATION THERAPY?

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Aims: The population over 65 years of age has increased in recent decades thanks to the decrease in mortality. This leads to a series of changes in the needs of the elderly, in the behavior and attitudes of the rest of the population towards them and, consequently, in age, which is a problem that occurs in old age. Most of the health requests come from this part of the society. Robert Butler first used the term ageism to define the systematic perpetuation of stereotypes and discrimination against people based on their age. The 2021 Global Age Discrimination Report (WHO) asserts that ageism has gradually become a societal problem. Age discrimination permeates many institutions and sectors of society, including those that provide health and social care. Rationing of health care services based solely on age is widespread. During the COVID 19 pandemic, age-discriminatory decisions were made, such as favoring younger patients in the ICU (intensive care unit) over older patients (Cesari JAMDA 2020). Another aspect of age discrimination relates to how health care providers communicate with older adults. A number of studies demonstrate that condescending and ineffective communication can shape the discourse between health care providers and older patients (Ambady 2002).

Methods: All operators were asked to complete an anonymous questionnaire (Q) on ageism (Fraboni1990, Donizzetti 2010) consisting of 25 questions plus 5 questions we added specific to the field of radiation therapy (RT). 37 Q were completed: 8 radiation oncologists, 5 medical physicists, 16 radiation therapy technicians, 5 nurses, 2 social workers, and 1 secretary. Analysis of the data, supported by psychology professors from the University of Bari, revealed that the younger subjects and the nurse category displayed some age-discriminatory attitudes. On the other hand, the physicians and physicists showed some archaic cultural beliefs, more influenced by contemporary society than by genuine ageist attitudes.

Conclusion: The need for knowledge about this problem is reflected in the prediction of less fear and more positive attitudes toward the elderly. The health personnel of RT are willing to dialog and establish a trusting and friendly relationship with the elderly patients. The ageist attitudes found were among the positive attitudes, while no negative ageist attitudes were found. Larger numbers would be needed for these initial and interesting *Results:*

P049

AGE RELATED EMOTIONAL DISTRESS IN CANCER PATIENTS DURING RADIO-ONCOLOGY TREATMENT

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Introduction: Emotional symptoms are present in all individuals at the time of the diagnosis, especially in the case of an oncological diagnosis. In this case, various factors intervene, cultural, social, previous experiences. There are many studies on emotional symptoms and cancer management in the literature. In recent years, the pandemic scenario has also been associated. Environmental factors, goals, and social context can influence emotional symptoms during treatment.

Objective: The aim of our study is to investigate prevalence and characteristics of emotional symptoms in a population of radio-oncological inpatients during COVID pandemic to better personalize the treatment.

Methods: We conducted an observational study in a population of patients admitted in the ward of Radiation

Oncology between April 2020 and June 2021. Patients were admitted to undergo cancer treatments or for acute disease or toxicities during treatments. Distress Thermometer/Problem List and Hospital Anxiety and Depression Scale were administered to each patient to investigate distress, anxiety and depression.

Results: we enrolled 133 patients, 32 were men and 101 were women. Mean age was 60 years old. We observed a higher prevalence of anxiety in women compared to men (OR 2.61, p 0.010). The correlation matrix showed a significantly positive correlation between patients' age and the HADS scale score for depressive symptoms. A t-test was then performed between the two age groups (age less than 65, age greater than or equal to 65) confirming higher depressive scores in older than younger patients ($p<0.05$).

Conclusions: The results highlight the importance of differentiating the psychological assessment and medical approachin accordance with the patient's age.

P050

IMPACT OF BREATHING AND IMAGE FILTERING ON RADIOMIC FEATURES EXTRACTED FROM 4D SIMULATION CT IN EARLY-STAGE NSCLC

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Aims: While 4D-computed tomography (CT) simulation represents a gold standard in stereotactic body radiotherapy (SBRT) for early-stage non-small cell lung cancer (ES-NSCLC), dedicated investigations on these images in radiomic studies are limited. This work aims to test the coefficient of variation (COV) of radiomic features across 10 respiratory phases; COV was also assessed after filtering methods were applied.

Methods: Seventy 4D-CTs acquired with the same scanner and acquisition parameters at a single Institution were retrieved. Pre-processing and features extraction were implemented using Pyradiomics v3.0.1. Features were subdivided into 7 classes, namely first order, gray level co-occurrence matrix, gray level dependence matrix, gray level run length matrix, gray level size zone matrix, neighboring gray tone difference matrix and shape. Null features in more than 90% of the cases in all respiratory phases were excluded. For each feature, the COV between the ten phases measurements was calculated for each patient [COV = (standard deviation/average) × 100]. Each feature is then represented by the average COVs among patients. The average COV was then classified as ≤5%, 5%<COV≤10%, 10%<COV≤20%, COV>20%.

Results: Almost 2000 features, mainly classified within the gray level co-occurrence matrix category, were extracted. Considering pre-processing methods, the majority of features derived from the wavelet (all permutations), lpb-3D and log-sigma filters (n= 744, 279 and 279, respectively). Qualitatively, COVs> 20% were observed across all categories and filters. Specifically, COVs>20% were more the most frequent in the gray level zone matrix and in the neighboring gray tone difference matrix categories. The application of pre-processing determined a different distribution of COVs, with a predominance of stable features (COVs≤5%) in the lpb-2D and lpb-3D methods, while the largest variability was observed when the logarithm and log-sigma filters were used (Figure 1).

Conclusions: Radiomic features show a significant range of variability across respiratory phases. In addition, as our results suggest, not only breathing but also the application of specific filtering techniques can affect features stability. While the impact of COVs in clinical prognostic modelling is being assessed by our group, we can affirm that these preliminary results have shed a light on the potentials of implementing 4D-based analysis in radiomic studies for ES-NSCLC.

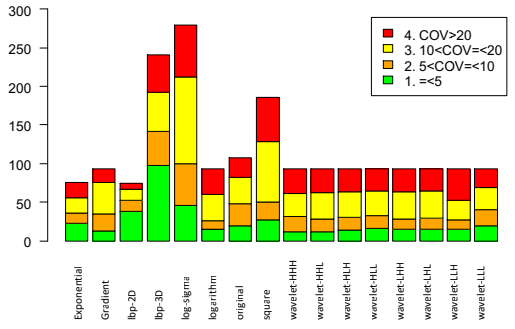

Figure 1. Distribution of coefficient of variation (COV) across the selected pre-processing methods.

P051

ABSTRACT NOT PUBLISHABLE

P052

VALIDATION OF AUTOCONTOURING FOR WHOLE BREAST RADIATION (WBRT) AFTER BREAST-CONSERVING SURGERY (BCS) FOR BREAST CANCER (BC): PRELIMINARY RESULTS OF A SINGLE CENTRE

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Aims: BC is the most frequent tumour in women and it represent about 50% of the workload of a RT department. The delineation of CTV and OAR could be very time-consuming and the inter-operator variability substantial. In last years some deep-learning autosegmentation software has been developed to improve efficiency and uniformity of RT structures. The aim of our study was to evaluate the results of an auto-contouring software comparing to manual delineation.

Methods: In May 2022, 25 female patients candidate to WBRT after BCS for BC were selected for the study. All patients underwent CT simulation in supine position; left and right breast, heart, left and right lung were automatically outlined directly on CT simulator using Siemens DirectORGANS 2.0. Then the same structures were also manually contoured by experienced RT oncologists, hidden the autocontours and recording manual delineation time. To evaluate the accuracy of autocontouring, the volumes were analysed using 3 different index: Overlap Index (OI), Dice Similarity Index (DSC) and Volume Difference (Dv). Among them, the closer OI and DSC are to 1, and Dv is to 0, the better is the outlining result.

Result: Efficacy of autocontouring was different among the structures. Overall OI and DSC was quite good for all the volumes, instead Dv was acceptable only for lungs and heart. Both lungs showed the best results of all the index, with average OI of 0,94 and 0,95, DSC 0,96 and 0,97 and Dv -0,04 and -0,06 respectively; moreover, OI and DSC was>0,9 in all the cases and Dv<0,1 in all but one. Very good results were recorded also for heart with an average OI, DSC and Dv respectively of 0,98, 0,92 and 0,16. Autocontouring of CTV and contralateral breast didn't reach a sufficient efficiency; only OI resulted with an average > 0,95, in no case a DSC > 0,9 was recorded and in just 2 patients Dv was better than 0,1. The median time of manual contouring was 41 minutes (range 32-68).

Conclusions: Our study showed good results in autosegmentation for WBRT with an excellent accuracy and efficiency for lungs and heart compared with manual outlining. Instead autocontouring of both breasts demonstrated heterogeneity, so major corrections need to be manually done to be acceptable for RT planning. In conclusion, autocontouring using Direct ORGANS 2.0 can be feasible and could play a role in both saving time and standardize RT structures for some OAR; all the volumes must always be assessed and approved by a RT oncologist.

P053

QUO VADIS, RADIOMICS? BIBLIOMETRIC ANALYSIS OF 10-YEAR RADIOMICS JOURNEY

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Aims: The aim of this work is to perform an unbiased, machine learning (ML) based bibliometric analysis on Radiomics 10 years after the first work on this topic became available to the scientific community.

Methods: Scopus electronic documents database was used as data origin. R code with Bibliometrix package was used for data analysis. Analysis of document categories, authors affiliations, country scientific collaborations, institution collaboration networks, keyword analysis, comprehensive of co-occurrence network, thematic map analysis and 2021 trend topics focus was performed.

Results: A total of 5623 articles and 16,833 authors from 908 different sources have been identified. The first available document was published in March 2012, while the most recent was released on the 31st of December 2021. China and USA were most productive countries with a prevalence of Single Country Publication for both. We identified five words clusters by co-occurrence network analysis based on top 50 authors' keywords, namely, Radiomics, computed tomography, radiogenomics, deep learning, tomography. The trend topics analysis, based on keywords frequency, for year 2021 further showed an increased interest in artificial intelligence (n = 286), nomogram (n = 166), hepatocellular carcinoma (n = 125), COVID-19 (n = 63) and X-ray computed (n = 60).

Conclusions: Our work clearly demonstrates the importance of ML-based bibliometric analysis to detect unknown pattern of data in Radiomics publications, highlighting potential developments to ensure knowledge dissemination in the field.

P054

CRITICAL EVALUATION OF RAPIDPLAN MODEL IMPLEMENTATION FOR PROSTATE CANCER PATIENTS

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Aims: Varian's Rapidplan (RP) is a Knowledge-Based Planning (KBP) algorithm which improves time

performance and evens out planning results from users with different levels of expertise. The purpose of this study was the implementation and validation of a prostatic cancer RP model and the comparison of the resulting plans with clinically and dosimetrically approved ones (gamma criterion of 2%/2mm).

Methods: In January 2022, a database of prostate cancer cases was created, including 24 patients treated with radical radiotherapy. For each patient the CT scan was taken and the structures revised according to the EORTC guidelines. This was done to improve uniformity of the contours and to match the number of Organs At Risk (OAR) considered in the RP model. The dosimetric and geometric information were extracted from each approved VMAT plan and the model was trained. The time performance and the clinical applicability of the model were studied by evaluating 5 plans from patients belonging to the RP model sample and 5 outside the sample. For each clinical case, a new plan was optimized using RP. A Student's T-test was performed to check the equivalence of the new plan and the clinically approved one. For each plan we evaluated D95% for the PTV, V36Gy, V49Gy, V63Gy, V70Gy for the bladder and V45Gy, V54Gy, V63Gy, V67.5Gy, V70Gy for the rectum. We calculated the mean values considering separately RP and approved plans, and performed the equivalence test between them.

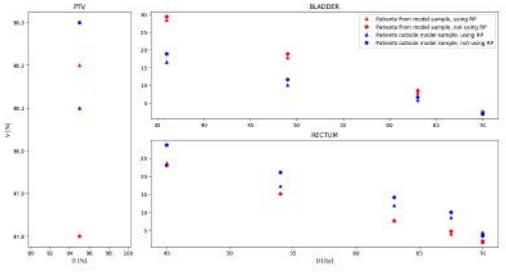

Figure 1.

Results: A RP model for prostatic cancer VMAT plans was successfully implemented. The resulting plans were clinically comparable or better than the clinically approved ones. The Student's T-test showed that equivalence hypothesis between RP and approved plans was never rejected (α=0.05). For OARs the lower equivalence probabilities were observed for low-dose constraints, with RP plans estimating on average smaller volumes for low doses. For PTVs the equivalence probability was low due to smaller standard deviations, however the absolute difference between approved and RP plans was lower than 0.6% of the prescription dose. For plans optimized with RP the results were given in 10-15 minutes, compared with the 20-30 minutes tipically required to optimize a VMAT plan without RP.

Conclusions: Time performance and clinical applicability of the implemented model allows the use of RP for future planning. Other RP models will be implemented for different RT sites to be routinely used in the clinical practice.

P055

MRI WITH DIFFUSION-WEIGHTED IMAGING IN IRRADIATED BONE METASTASES

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Aims: Bone metastases (BMs) occur in about 50% of cancer patients (pts) and cause a significant reduction in quality of life, producing pain. Accurate staging for BMs is utmost importance in determining appropriate treatment and prognosis. Magnetic resonance imaging (MRI) is considered the most sensitive technique to detect BMs. DWI is based on the evaluation of microscopic movements of water at the cellular level, providing quantitative (*e.g.*, apparent diffusion coefficient (ADC)) and qualitative information. Radiotherapy (RT) remains the mainstay for treatment of painful bone metastases and DWI is an efficient method to differentiate good and poor responders to radiotherapy. Aim of the study is to evaluate the prognostic role in term of pain control of DWI and ADC sequences in pts with BMs treated with palliative RT.

Methods: Between June 2021 and May 2022, 34 pts (24 male and 10 female), median age 68 years (range: 50-80) were treated with palliative RT for 36 BMs. All pts had MRI before RT (between 7 days) - MRIpre- and 30 days (5 days) after the end of the RT - MRIpost. Pain level will be defined using the NRS scale before RT and 30 days after the end of RT. To calculate the ADC average of each lesion, a single circular ROI was drawn on each section of the tumor displayed on the ADC map image. The various ROIs were then copied onto DWI for all assumed b values. Maintaining the same positions and the same magnitudes of the ROIs in the postMRI investigations

Results: Pain reduction was recorded in 12 pts (35%) at the end of RT and in 17 pts (51%) after 30 days. The mean and median of the ADC maps for the 34 BMs at the MRIpre were 1035 and 853, respectively; at the MRIpost were 1322 and 1053, respectively. The mean and median of the DWI maps at the MRIpre were 1195 and 822, respectively; at the MRIpost were 552 and 422 respectively. At univariate analysis the pain response assessed at the end of RT correlates with the delta DWI ($p = 0.004$) and with the delta ADC ($p = 0.0$); the pain response assessed at 30 days after the end of RT correlates with the delta DWI ($p = 0.002$) and the delta ADC ($p = 0.0$) Conclusion: DWI-MRI sequence is mandatory for evaluation of BMs

pts treated with RT. More pts and data are needed to evaluate the prognostic role of MRI not only in terms of response to the treatment according to RECIST 1.1 criteria but also in term of pain control

P056

GROSS TUMOUR VOLUME DELINEATION WITH FUNCTIONAL IMAGING IN NON-SMALL CELL LUNG CANCERS: 99MTC-MIBI SPET/CT AND 18F-FDG PET/CT

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Azienda Scaligera Ospedale Mater Salutis [1]UOC di Radioterapia e Medicina Nucleare; [2]UOC Radiologia, Italy

Aim: We compared the diagnostic accuracy of 99mTc-MIBI SPECT/CT in patients with non-small lung cancer who had a positive 18FDG PET/CT scan. Functional imaging was used to delineate gross tumour volume (GTV) for both primary lung lesions and lymph nodes.

Methods: Ten patients with clinically and radiologically advanced primary non-small cell lung cancers (age range: 75-86 years) were examined with 18FDG PET/CT and MIBI SPECT/CT within two weeks of each study. MIBI imaging started 10 minutes after intravenous tracer administration with SPECT/CT of the thorax. Functional imaging served to shape the radiotherapy planning with GTV. All patients were submitted to definitive VMAT radiation therapy because of their medical and surgical ineligibility due to comorbidities. MIBI SPECT/CT imaging was repeated at the end of radiotherapy to evaluate early response to treatment. The PET, SPET and co-registered CT findings were visually examined. Ratios of lesion to contralateral area were calculated and standard uptake values (SUVs) of lung lesions and mediastinal lymph nodes were generated in MIBI SPECT/CT and 18FDG PET/CT. Spirometry data was previously controlled and then patients were submitted to radiation treatments. Mono isocenter VMAT plans with 6 MV rays, using two coplanar semiarchs were calculated by Pinnacle, trying to avoid as much as possible the contralateral lung (50 Gy in 20 fractions, VERSAHD).

Results: There were no discordant results between the two tracers. All patients had positive PET and SPET findings, GTV were similar using both tracers. Functional imaging was very useful in patients with extensive tumour that was not easily distinguishable from any concomitant lobar atelectasis and helped the radiation planning. Spatial resolution and SUVs values were higher with PET/CT imaging and FDG tracer. MIBI and FDG imaging had the same diagnostic sensitivities and specificities in evaluating the primitive lung lesions and the suspected lymph node metastases. Functional GTV with MIBI and FDG differed by more or less 8-11 cc.

Conclusion: 18FDG PET/CT and 99mTc-MIBI SPECT had comparable results in these patients with advanced NSCLC, both tracers are useful tool for staging and radiation therapy planning. 99mTc-MIBI SPECT could be an alternative imaging modality to 18FDG PET/TC when the waiting lists for the diagnostic test are too long and there is an urgent need to carry out a radiation treatment plan or patients are unable to reach the hospitals with PET/CT facilities.

P057

AUTOMATED HIGH DOSE CTV DELINEATION IN HEAD AND NECK RADIOTHERAPY. OUTCOMES OF A PET-CT BASED DIRECT PLANNING PROTOCOL

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Aims: We report treatment planning implications and clinical outcome of an automated target delineation (for high dose clinical target volume - HD-CTV) based on a simulation PET-CT (sPET-CT) and direct planning protocol in head and neck (H&N) cancer radiotherapy (RT).

Method: From January 2018 to May 2020, twenty-four H&N cancer patients underwent to an optimized procedure of sPET-CT in RT set-up (flat top, mould), using a specific PET acquisition protocol (2 beds, matrix 400x400, 6 minutes/bed). Gross tumor volume (GTV) was delineated using an automated threshold method at 40% of the intralesional SUV max. HD-CTV was obtained adding a 9-mm isotropic margin, respecting anatomical boundaries. A 3-mm margin was added to generate the planning target volume. Volumetric modulated arc therapy (VMAT) plans were designed by including also elective nodal stations as indicated. Early clinical outcomes in terms of complete response (CR), partial response (PR) and progression disease (PD) were assessed with PET-CT within six months after treatment completion. Clinical records were analyzed to assess late clinical outcomes.

Results: All 24 enrolled patients showed GTV evidence on sPET-CT at baseline. Subsites involved were: oral cavity (5), oropharynx (7), larynx (8), hypopharynx (2), nasopharynx (1) and ethmoid sinus (1). The stage of disease ranged widely. HD-CTV dose prescription ranged from 66 to 70 Gy delivered with SIB. Concurrent chemotherapy was administered in 17/24 patients. All patients completed RT. At the early 6 months median follow-up all patients undergone at least one PET-CT evaluation; 18/24 patients showed CR, 4/24 showed PR and 2/24 experienced PD. To April 2022, with a median follow up of 32 months, 16/24 patients experienced no local

recurrence of disease, 8 patients had a local progression/relapse of disease. Multivariate Cox regression analysis was performed, the early PET-CT response is a variable associated to late outcome of local progression/relapse HR 6.7 (95% CI 1.6 – 27.6) P 0.009.

Conclusions: In our cohort, sPET-CT could be considered an optimization in RT planning. The threshold SUV based automated delineation resulted to be a simple and interobserver homogeneity carrier contouring method. H&N patients undergone to sPET-CT direct planning protocol showed good early responses to treatment which resulted to be associated to late disease local control. Larger and more homogeneous series of patients are needed to confirm these data.

P058

CURRENT PRACTICES AND PERSPECTIVES ON THE INTEGRATION OF CONTRAST AGENTS IN MR-LINAC CLINICAL PRACTICE: A WORLDWIDE SURVEY

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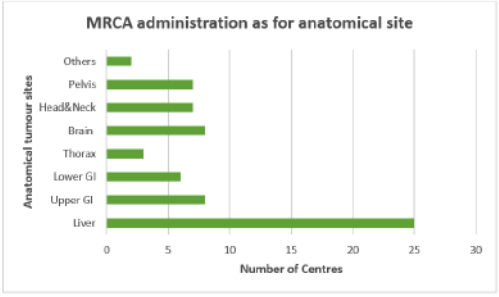
Aims: The introduction of magnetic resonance guided radiotherapy (MRgRT) has led to an improvement in the therapeutic workflow of radiotherapy (RT) treatments thanks to the better visualization of therapy volumes assured by the higher soft tissue contrast. Despite the introduction of this innovative technology and numerous , little is still known about the implementation of the use of MR contrast agents (MRCA) in MRgRT planning. MRCA could improve the segmentation of the target as well as reduce inter-observer variability and enable dose escalation protocols. The aim of this survey is to investigate CA utilization among centres that implemented MRgRT technology.

Method: In September 2021, we conducted an online survey consisting of a sixteen-question questionnaire that was distributed to the all the hospitals around the world equipped with MRgRT technology. The questions were divided into 3 sections: screening of the centre; type of MRCA used and clinical applications with treated anatomical sites; opinion on the inclusion of MRCA guidelines. The questionnaire was developed by two Italian 0.35 and 1.5T MR-Linac centres and was validated by four other collaborating centres, using a Delphi consensus methodology.

Results: The survey was distributed to 52 centres and 43 centres completed it (82.7%). Among these centres, 23 institutions (53.5%) used the 0.35T MR-Linac system, while the remaining 20 (46.5%) used the 1.5T MR-Linac system. According to reports obtained from this survey, 25 (58%) of the centres implemented the use of MRCA for MRgRT imaging. Gadoxetate (Eovist; Primovist) resulted to be the most used MRCA (80%) and liver results the most common site of application (58%). Over 70% of partecipants agreed or strongly agreed with the need for international guidelines. Table 1 summarizes the anatomical sites of MRCA use for all the responding centers.

Conclusions: Based on the results from this survey, future research will be necessary for the development of protocols for optimised procedures with the aim of formulating guidelines for standardizing the use of CA in the MRgRT workflow, exploring its added benefit and possible toxicity related issues.

Table 1.



P059

WHAT IMAGING AND PLANNING TECHNIQUES ARE RECOMMENDED FOR THE STEREOTACTIC TREATMENT OF ARRHYTHMIAS (STAR)? A SYSTEMATIC LITERATURE REVIEW

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Aims: Stereotactic treatment of arrhythmias (STAR) is receiving increasing interest as non-invasive and well-tolerated therapy. However, international consensus guidelines on STAR planning and delivery are lacking.

Therefore, the purpose of our review is to summarize and analyze the available evidence resulting from planning studies on STAR.

Table 1. Characteristics and main findings of the analyzed studies.

Author/year	Setting	Study characteristics	Main findings
Wang L et al/2018	VT	**Objective:** to dosimetrically analyse 3 treatment platforms for STAR **Methods:** The target volume of the first patient was studied and treatment plans were developed on 3 platforms: CyberKnife® G4 system with iris collimator (Plan #1), CyberKnife® M6 system with InCise 2 multileaf collimator (Plan #2) and Varian TrueBeam STx with HD 120 MLC and 10MV FFF beam (Plan #3: coplanar VMAT; #4: noncoplanar VMAT). Thereafter, the plans were compared for isodose prescription, plan compliance index, dose gradient, and dose to OARs. Monitor units (MU) and treatment time were analysed as parameters of treatment efficiency. According to plans #1-4, 8T (25 Gy) was delivered on PTV at isodose lines 75.0%, 84.0%, 84.3%, and 84.9%.	**Results:** • Compliance indices: 1.15, 1.18, 1.05, and 1.85; dose gradients: 3.02, 3.42, 3.61, and 3.73, for plans#1-4. • Doses to the OARs were within constraints (lung, stomach, bowel and oesophagus). • The MUs for plans #1-4 were 27,671, 16,522, 6,275, and 6,004, with total treatment time/beam delivery time of 99/69, 93/31, 37/7, and 59/6 minutes, respectively. • For VMAT, gated beams, a duty cycle of 80%, a dose rate of 2,400 MU/minute, and an additional 10 minutes for each further arc were considered. **Conclusion:** The most conformal plan was delivered with CyberKnife® M6 with InCise 2 collimator with reduced MU and treatment time compared to his plan. However, TrueBeam plans (Plan#3-4) allowed treatments with less MU and time compared to CyberKnife Plans (Plan#1-2).
John RM et al/ 2018	VT	**Objective:** to review literature data on cardiac STAR technique and collateral exposure to RT.	**Results:** Electrocardiographic imaging system with 256 electrodes (ECGI) gives more accurate mathematical reconstruction of potentials at the surface of the heart compared to E-ECG. **Conclusion:** to assess the risk of toxicity after STAR is important to model the dose exposure outside the target
Weidlich GA et al/ 2018	VT	**Objective:** to compare VT treatment techniques with 4 different accelerators: Accuray CyberKnife, Varian TrueBeam, Elekta Infinity and Varian Edge. **Methods:** The 4 treatment techniques were examined for their effectiveness in treating the target.	**Results:** LINACs were better at sparing OARs and ensuring efficient treatment, due to smaller amount of monitor units: 6,400.7 MU (Varian TrueBeam) vs 11,725.6 MU (CyberKnife) and shorter treatment time (9.5 min vs 34 min, respectively). However, CyberKnife spares nearby structures with more consistent dose gradients at the target periphery. Both were efficient in coverage and adequate target conformation. **Conclusions:** both CyberKnife and standard linacs are adequate for STAR.
Ghobarah A et al/ 2019	VT	**Objective:** to analyse the correspondence between epicardial exit of VT and critical targets for STAR **Patients:** 8 patients were included and 9 VTs were investigated by analysing the diastolic pathway and VT exit sites (epicardial and endocardial). **Treatment:** The cardiac map was obtained using a 312-dipole endocardial balloon and a 312-dipole epicardial clocking array.	**Results:** • Mapping of the diastolic pathway in the endocardium (median length: 56 mm; interquartile range [IQR]: 28 mm). • Tachycardia cycle length range: 210-500 ms. • Early VT exit site for 8/9 VT in the endocardium and 9/9 VT in the epicardium. **Conclusion:** ECG-based identification of epicardial exit site can be distant from STAR target
Knutsen RC et al/ 2019	VT	**Objective:** to report the steps in the treatment pathway and dose-volume characteristics of the prospective ENCORE-VT study for cardiac radioablation. **Methods:** 50 patients who received 25 Gy (single fraction) in a phase-II trial were included. PTV, RSD (ratio of PTV in the 12.5-Gy isodose), mean/ramp arith ratio and gradient measurement values were analysed over time. Outlier values in the dose-volume histogram (DVH) for PTV and organs at risk and median doses to the heart were studied.	**Results:** • GTV volume: 25.3 cc (range 11.5-54.9 cc) • ITV volume: 30.1 cc (range 17.7- 81.6 cc) • PTV volume: 97.9 cc (range 66- 208.5 cc) • In 2 patients deviation from the threshold from the DVH data of the beam enteso-PTV, oesophagus and stomach (but clinically acceptable). • In the last treated patients: reduced RSD, gradient measure, and treatment time **Conclusion:** over the course of the trial, PTV volumes were significantly decreased. OARs constraints were met for all subjects.
Hohmann S et al/ 2020	AR	**Objective:** to guide target definition on EAM maps. **Methods:** using a free open-source software 3D Slicer, map points were transferred to CT and then the target volume was defined on CT.	**Results:** Alignment map to the CT showed a mean displacement of 5.1 mm. **Conclusion:** A new planning workflow allows accurate integration of EAM with planning CT
Cuiying Z et al/ 2020	VT	**Objective:** To investigate the heart motion using cardiac-gated computed tomography and to identify planning margins. **Methods:** Contrast-enhanced CT scans were acquired from 30 apnoea patients and the left ventricle, right ventricle, ascending aorta, ostium of the right coronary artery, left coronary artery, and left anterior descending artery were contoured at each phase of the cardiac cycle. For each structure, displacements from their mean positions were measured while, for the left and right ventricles, mean volumes and maximum and minimum ratios were studied.	**Results:** • Displacements were variable among cardiac structures but < 5 mm for most of them. left and right ventricle average volumes ranged from 191.25 to 429.51 cc and from 55.76 to 286.98 cc, respectively. • Ratios of maximum to minimum volumes within a cardiac cycle ranged from 1.15 to 1.58 for left ventricle and from 1.34 to 1.84 for right ventricle. **Conclusion:** The calculated heart movement displacements were within 5 mm, despite variable among cardiac structures. Planning margins should be defined based on the target position.
Paan J et al/ 2020	VT	**Objective:** to investigate the cardiac synchronised VMAT as a possible technique to reduce the STAR dose to healthy tissues **Methods:** The cardiac synchronized VMAT plan was derived from a conventional VMAT plan and was used on a Varian TrueBeam linear accelerator. The original VMAT plan was divided into 3 phases each of them consisting of alternating beam-on and beam-off segments synchronised at a sample heart rate.	**Results:** The dose distributions between the original plan and the cardiac synchronized VMAT plan were in agreement. A treatment delivery technique synchronised to the heart movement is more precise and advantageous. **Conclusion:** VMAT plan with cardiac synchronized technique showed better agreement between calculated and delivered dose.
Witteveli S et al/ 2020	VT	**Objective:** to test STAR with photon and proton beams, applying the robust optimization technique **Methods:** A patient underwent upwise CT and 2 plans with photons and protons (25 Gy in a single fraction) were compared with conventional PTV- and robust-optimized plans. Setting and target motion errors due to cardiac motion and breathing were considered.	**Results:** • Robust optimization plan with photons: reduction in the mean dose to the heart of about 25% and to the left lung of 1.4 to 1.8 Gy for a 5-beam configuration and from 4.1 to 2.9 Gy for a 9-beam configuration • Proton robust optimization plan: reduction to the heart from 7.3 GyE to 5.2 GyE and to the left lung from 2.9 GyE to 2.2 GyE. **Conclusion:** A robust optimization planning allowed to deliver RT more safely to the healthy cardiac tissue.
Abdel-Kafi S et al/2021	VT	**Objective:** To analyse inter-observer agreement in defining GTV on ECT based on EAM data in patients with VT undergoing STAR. **Methods:** EAM data (two-dimensional surface) were exported and manually merged by 3 operators who defined the GTV on CT images. The influence of EAM data availability and inter-observer agreement were evaluated.	**Results:** • CCT-EAM median distance after registration for the 3 operators: 2.7 and 3.0 mm, respectively (p: 0.9). • significant difference between the 2 GTVs (8 versus 19 cc) • lower agreement in GTVs on the lateral wall • better agreement in recording of EAM-based outlines when mapping at least 3 heart chambers. **Conclusions:** Detailed EAM-mapping of at least 3 heart chambers improves CCT-EAM co-registration and inter-observer concordance.
Redo Heggemann J et al/ 2021	VT	**Objective:** to guide target CTV identification on the basis of EAM and to evaluate interrunter variability. **Methods:** 9 patients were studied by 5 university centres. CTVs were contoured independently by analysing VT sites on EAM maps and transferring them to the CT. The consensus structures were subsequently defined by the centers.	**Results:** • Between-centre variability, regarding VT site on EAM, was greatest for 2 cases. • CTV volum ranges: 6.7- 12.8 cc, 5.9 - 79.9 cc, and 9.6- 86.3 cc. • Surface areas ranges: 1087- 3265 mm², 1077- 4600 mm², and 1620- 4179 mm². • Conformity index ranges for CTVs: 0.2- 0.88, 0.02- 0.85, and 0.02- 0.88 considering the consensus CTV as the reference (conformity index: 1). **Conclusion:** Disagreement was found in the definition of CTV on EAM and CT, particularly during the transfer between EAM and FCT. Coherent methods are needed between centers to transfer CTVs from EAM to CT.
Bassquette I et al/ 2021	VT	**Objective:** to optimize geometric aspects, prescription methods, and delivery in Linac-based STAR of the VT. **Methods:** PTV from a real patient undergoing STAR was used. * geometric aspects: 3 TPs were compared (75% isodose prescription) with different number and extension of the arches and with various table rotations * prescription mode: the best "geometric" plan was used to compare prescriptions at the 75%, 70%, 65%, and 60% isodose * dose delivery: VMAT-FFF treatments with 6 MV and 10 MV energies were compared	**Results conclusions:** optimal geometry: 2 arcs (with couch degree of 30°-330°); optimal prescription: 75% isodose lines; faster delivery: 10 MV FFF (but not suitable for ICD patients)
Cha MJ et al/ 2021	VT	**Objective:** to test STAR planned with DIBH to reduce stomach toxicity **Methods:** 1 patient with intractable VT and history of cardiac valve surgeries was treated with STAR. The delineation of the target and treatment planning were studied to treat the trigger of the VT in the left ventricle inferior scar near the stomach. Distances between target and stomach were assessed on 4 planning CT scans: DIBH, full inspiratory, and four-dimensional (4D) apnea without and with abdominal compression.	**Result:** Greatest distance between target and stomach and satisfactory dosimetric parameters were achieved in CT with DIBH. No complications were recorded. **Conclusions:** DIBH allows increased distance between STAR target and stomach
Dickerman RM et al/ 2021	VT	**Objective:** to report the first case of a patient treated with STAR **Methods:** In a center without experience on STAR, one patient with refractory VT underwent 4D-CT simulation and the target volume was contoured on the basis of information from echocardiogram, cine MRI, and the EAM using the CARTO®3 system. STAR (25 Gy, single fraction) was delivered.	**Results:** STAR was delivered the day after consultation **Conclusion:** complex STAR planning requires strong multidisciplinary collaboration
Knybel L et al/ 2021	VT	**Objective:** to assess the respiratory and cardiac-induced motion of a ICD lead as surrogate of the heart during STAR **Patients:** 20 patients previously treated with STAR for VT **Methods:** Motion data were collected. To quantify the excursion and margin expansion in all directions to cover 90% or 95% of all amplitudes, the following parameters were assessed: ICD-lead movement, intrafraction amplitude variability, correlation error between ICD lead and external markers on the patient's chest.	**Results:** • Movement amplitudes: mean value = 5.0 ± 2.6, 3.4 ± 1.9, and 3.1 ± 1.6 mm in the SI, LL, and AP directions, respectively. • Intrafraction amplitude variability: mean values= 2.6 ± 0.9, 1.9 ± 1.2, and 1.6 ± 0.8 mm in the SI, LL, and AP directions, respectively. • Margins: 9.4, 6.7, and 5.5 mm in the SI, LL, and AP directions, respectively, to cover 95% of the ICD lead motion amplitudes. • Correlation error: mean value = 2.2 ± 0.9 mm **Conclusions:** optimized treatment margins were proposed.
Q M Rinks C et al/ 2021	VT	**Objective:** to evaluate the possible advantages, in STAR of VT, of treatment arches trajectory optimization using the 4π technique (minimization of the overlap of PTV and OARs in the trajectory of the beams) to reduce OARs irradiation. **Method:** PTV (prescribed dose: 25 Gy) and OARs were delineated on the CT of 15 patients. The 4π technique versus treatment with 2 complete coplanar arches were compared. Maximum, mean, and median dose to the OARs were compared.	**Results:** • PTV: no significant differences in terms of maximum dose and of dose homogeneity. • cardiac structures: significant reduction of mean and median doses with 4π technique (no reduction of maximum dose) • non-cardiac OARs: significant reduction of maximum, mean and median doses with 4π technique **Conclusions:** 4 π technique is particularly useful in STAR of VT.
Sindone M et al/ 2021	VT	**Objective:** to describe the current standard of VT radioablation.	**Results:** • Multiple techniques are suggested to localize the arrhythmogenic target: Contrast-enhanced ECG-gated Cardiac CT, Cardiovascular Magnetic Resonance, Nuclear Imaging as SPECT or CMG-PET, Invasive Cardiac Mapping with catheters, non-invasive Cardiac Mapping with surface electrodes; • Moreover, the following planning techniques are recommended: - Free breathing CT with IV contrast and 4DCT as simulation; - Fusion of contrast-enhanced cardiac CT scan and 4DCT for the correct definition of the arrhythmic ventricular scar based on heart walls thinned by more than 50%; - ITV contouring based on the maximum extension of respiratory and cardiac motion in all directions; - PTV: expansion of 5-7 mm of the ITV, eventually anisotropic. **Conclusions:** the recommended dose is 25 Gy in single fraction, preferably with FFF delivery and cone-beam CT to align the patient to beam and target.

Legend: AR: arrhythmias; ECT: cardiac computed tomography; CT: computed tomography; DIBH: deep inspiration breath-hold; EAM: electroanatomical mapping; ECG: electrocardiogram; FFF: filter-flattening-free; ICD: implantable cardioverter defibrillator ; LINAC: linear accelerator; MRI: magnetic resonance imaging; OaR: organs at risk; PCT: planning computed tomography; RT: radiotherapy; SPECT: Single-photon emission computed tomography; STAR: stereotactic arrhythmia radioablation; VMAT: volumetric modulated arc therapy; VT: ventricular tachycardia

Method: A literature search was conducted on PubMed on 25 January 2022. The search strategy was as follows: ("stereotactic" OR "SBRT" OR "radiosurgery") AND ("arrythmia" OR "tachycardia"). We included only planning studies on STAR, published in English, with no time limits.

Results: Seventeen papers were included: 11 studies on target definition and 6 articles on planning techniques and optimizations. Main findings of the included papers are summarized in Table 1. Briefly, several techniques were proposed to localize the arrhythmogenic target but combination of contrast-enhanced cardiac CT and 4D-CT simulation were regarded as optimal. Largely variable target volumes were reported being GTV, CTV, PTV and surface areas ranges as follows: 8-54.9, 5.9-79.9, 66-208.5 and 1077-9500 mm^2, respectively. Regarding the critical problem of heart movements, the analyzed studies reported < 5 mm displacement of cardiac structures while one study reported 5.0 ± 2.6 mm, 3.4 ± 1.9 mm, and 3.1 ± 1.6 mm mean motions in the SI, LL, and AP directions, respectively. These figures can be useful to define an ITV to which a 3-7 mm expansion should be added. Another proposed solution to overcome the target motion issue is to plan STAR with cardiac synchronised VMAT. Moreover, several studies confirmed the safety of delivering 25 Gy in single fraction without exceeding the OaR constraints. Furthermore, treatments delivered by linear accelerators require a smaller amount of monitor units compared to CyberKnife. Finally, treating the cardiac substrate in DIBH may reduce the risk of gastric toxicity.

Conclusions: A strong multidisciplinary collaboration is required and consistent planning methods are needed between centres. STAR adherence to Oar constraints, and therefore treatment safety are feasible through the use of advanced planning and delivery techniques.

P060

STEREOTACTIC TREATMENT OF ARRHYTHMIAS (STAR): A SYSTEMATIC REVIEW OF PRECLINICAL STUDIES

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Aims: Several treatments are available for the treatment of arrhythmias, a common cause of morbidity and mortality. In recent years, in order to provide arrhythmic patients with effective and non-invasive treatment, the possibility to use stereotactic radiotherapy in this setting has been increasingly tested. Several preclinical studies have focused on evaluating the efficacy and safety of stereotactic treatment of arrhythmias (STAR). The aim of this review is to summarize the main preclinical evidence on STAR.

Table 1. Characteristics and main findings of the analyzed studies.

Authors/ year	Setting	Study characteristics	Main findings
Amino et al/ 2006	AR	**Objective:** to test the role of connexin 43 (a gap junction protein regulating the cell-to-cell communication in the heart) in the setting of RT for AR. **Methods:** a microsphere injection into the coronary arteries of 24 rabbits was performed causing a myocardial infarction. Other 24 rabbits without infarction were considered as controls. A heavy ion single fraction of 15 Gy was delivered 2 weeks after.	**Results:** • Increase of levels of connexin 43 in both groups after RT • Reversed reduction of connexin 43 signals in infarcted hearts and related electrical function after RT. **Conclusion:** RT increases connexin 43 levels and enhances intracardiac conductivity.
Amino et al/ 2010	AR	**Objective:** to study time and dose-dependent STAR effects on connexin 43 levels. **Methods:** 45 healthy hearts of rabbits were treated with RT (5-15 Gy). Five not irradiated rabbits were considered as control.	**Results:** • Increase of connexin 43 levels after 15 Gy • Dose dependent increase of connexin43 levels after RT ≥ 10 Gy. • No in vivo late toxicity after 1 year **Conclusion:** A single 15 Gy fraction of increases connexin 43 and gap junctions in myocardial cells.
Sharma A et al/ 2010	AR	**Objective:** to evaluate the electrophysiological efficacy of STAR and histopathological consequences. **Methods:** 14 mini pigs under general anaesthesia were subjected to CT scans and EAM with the CARTO system. STAR (dose range: 25- 50 Gy) was delivered with the CyberHeart system, targeting the cavotricuspid isthmus, AV node, pulmonary vein-left atrial junction, or left atrial appendage. From 25 to 190 days after treatment, electroanatomical voltage mapping and transesophageal echocardiography was repeated, when possible.	**Efficacy:** • Minimum dose to obtain an electrophysiological effect (absence of spontaneous arrhythmias): 25 Gy • Reduction less than 0.05 mV in the left pulmonary vein atrial junction and the left atrial appendage. No spontaneous AR were noted. **Safety:** No radiation damage adjacent to the target and clear histological evidence of irradiation in target areas **Conclusions:** the minimum STAR dose to achieve an ECG effect of an animal model is 25 Gy.
Gardner et al/ 2012	AF	**Objective:** to report a treatment experience on cardiac targets with CyberKnife **Methods:** Four animal models (dogs and pigs) were treated with 20-35 Gy in a single fraction directed on pulmonary vein ostia. A TLD and MOSFET dosimeters were employed to measure the dose on the epicardial surface and on the esophagus.	**Results:** • TLD dosimeter measure: 5% less than expected dose on epicardium • MOSFET dosimeter measure: 6% less than expected dose on coronary sinus • Dose on esophagus: 25% less than expected **Conclusion:** Treatment with CyberKnife is accurate on target and esophagus.
Blanck et al/ 2014	AF	**Objective:** to study the histological effect on heart after STAR **Methods:** 9 mini-pigs underwent MRI and electrophysiological exam. The right superior pulmonary vein antrum (volume 5-6 cc) received (random) a sgle-fraction doses of 0 and 17.5-35 Gy. MRI, electrophysiological and histopathological exams were performed 6 months after RT.	**Results:** • Transmural scarring on hearts with RT dose ≥ 32.5 Gy • Dose-dependent fibrosis • Unimpaired myocardial function • Safe treatment for adjacent structure **Conclusion:** A non-invasive method to treat AF inducing myocardial scarring has been demonstrated.
Bode et al/ 2015	AF	**Objective:** to report the electrophysiological efficacy of STAR and histopathological consequences. **Methods:** 8 mini-pigs underwent STAR (dose range 22.5-40 Gy) on pulmonary vein antrum after an electrophysiological exam, which was repeated following the treatment together with an histological exam.	**Results:** • Atrial excitation after radiations of the pulmonary vein (veno-atrial conduction) • Decreased pulmonary vein electric waves after 6 months • 40 Gy-RT: complete block of atrio-venous conduction • Doses > 30 Gy: transmural scarring of the target tissue • Doses ≥ 40 Gy: extended scarring on all the circumference **Conclusion:** Radiotherapy on pulmonary vein could be used to treat AF. However, clinical application could be limited by high doses.
Lehmann H et al/ 2015	AR	**Objective:** to test in vivo the catheter free ablation for AR using ^{12}C beams **Methods:** 4 porcine hearts were explanted and reperfused. A CT and a treatment planning were performed after positioning of fiducial clips. Doses of 70, 90 and 160 Gy were delivered on AV nodes of 3 hearts, the fourth was considered as control. After irradiation, positron emission tomography-computed tomographic scans were acquired.	**Results:** • None induced arrhythmic events • No myocardial damage • Regular rhythm observed with a dose of 160 Gy **Conclusion:** Carbon ions beams using ^{12}C beams could be implemented because of its feasibility in this study.
Prall M et al/ 2015	AR	**Objective:** to report the main findings and acute side effects of AV nodes irradiation with ^{12}C beams **Methods:** 4 porcine hearts were explanted and reperfused. CT and treatment planning were performed after positioning of fiducial clips. Doses of 80 Gy and 160 Gy in 16 fractions and 90 Gy in 18 fractions were delivered on AV nodes of 3 hearts, the fourth was considered as control. After irradiation, positron emission tomography-computed tomographic scans were acquired.	**Results:** • No changes in AV conduction with the lowest dose • No myocardial damage • No acute events after irradiation **Conclusion:** Heavy ion irradiation could be delivered on a cardiac target without acute effects
Lehmann H et al/ 2016	AR	**Objective:** to test heavy ion irradiation in treatment of AR in porcine hearts **Methods:** 34 pigs received (randomly) RT on different cardiac substructures (doses: 25-40-55 Gy) and 3 pigs were considered as controls. After irradiation, positron emission tomography-computed tomographic scans and ultrasound images were acquired. An histopathological exam was performed.	**Results:** • Deceleration and interruption of cardiac conduction with doses of 40-55 Gy • Apoptosis after 3 months of treatment but not after 8 months **Conclusion:** Heavy ion irradiation is a feasible treatment to give cardiac lesions that interrupt conduction in the heart
Amino M et al/ 2017	AR	**Objective:** to test the effect of ^{12}C beams irradiation on ischemic hearts **Methods:** a myocardial infarction has been inducted in hearts of 6 dogs using injection of microspheres in coronary arteries. Four dogs underwent irradiation (15 Gy) and four were considered as controls. After one year, the following exams were conducted: signal-averaged ECG, echocardiograms and immunohistochemical tests.	**Results:** • QRS duration: 118 ± 1.4 ms in the control group, 109 ± 6.9 ms in the irradiated group. • Reduced AR inducibility of 25% in irradiated group compared to 100% in the control group • Increase of 24-45% of connexin 43-expression in irradiated group. • Intubated left ventricular ejection in the two groups **Conclusion:** ^{12}C irradiation reduced AR inducibility in ischemic hearts increasing connexin 43 levels after 1 year
Lehmann et al/ 2017	AR	**Objective:** to describe the treatment with RT on atrioventricular junction **Methods:** 30 pigs were randomized to receive RT (16, 50, 80, and 95 Gy) on the atrioventricular junction.	**Results:** • Target volume (mean value): 2.5 ± 0.5 mL • Complete atrioventricular block in 6/7 irradiated pigs for all dose groups • No short-time toxicity • Histological consequences visible outside the target **Conclusion:** Histological injury to myocardial tissue is evident with doses above 35 Gy. The conformity of the target was not obtained as expected.
Rehan et al/ 2017	AR	**Objective:** to report the method to ablate atrioventricular node with RT in pigs **Methods:** Pacemakers were implanted in 5 pigs. CCT was performed to visualize the atrioventricular node. Doses of 35-40 Gy were delivered on atrioventricular node and data from pacemakers were analyzed each week.	**Results:** • Transition to complete AV conduction block in all pigs • Fibrosis in the target area, not in adjacent regions • No myocardial damage **Conclusion:** Safety and histological effects of RT to treat AR have been demonstrated in pigs.
Jin YC et al/ 2018	AF	**Objective:** to evaluate the efficacy and safety of STAR in adult canine atrial pigs **Methods:** 37 adult canines and 2 adult pigs were included in this study and fiducial markers were placed. Computer angiography 3D anatomical rendering of the left atrium was performed and a treatment plan targeted to the right upper pulmonary vein was developed. 4 treatment doses (10, 20, 25, and 35 Gy) were administered to 4 cohorts. Electrophysiological tests was performed during 3-6 months of follow up and 2 subjects were studied with histopathological examination.	**Efficacy:** at electrophysiological study and macroscopic pathological analysis: • 100% effect (entrance and exit block and low voltage in the target area) in all pulmonary veins treated at ≥ 35 Gy and 25 Gy; partial effect at 20 Gy (80%) and at 15 Gy (50%) • Presence of transmural scar in the irradiated area at histopathological examination in the 2 subjects. **Safety:** No adverse events and no damage in normal tissue adjacent to the target. **Conclusion:** STAR in cats up to 35 Gy is in animal models.
Klein S et al/ 2020	VT	**Patients:** 4 explanted hearts of non-ischemic cardiomyopathy patients in the context of transplantation that received STAR (total of 11 patients) were studied. **Treatment:** STAR with a single fraction dose of 25 Gy was delivered to the scar area. The time from STAR to explantation ranged from 12 to 258 days. Target areas were compared with anatomical sample. A histological analysis of the tissue was performed.	**Histological outcome:** in all patients subendocardial necrosis surrounded by a border of fibrosis; cytoplasmic vacuolization in myocytes of the surrounding myocardium and fibrosis were observed in two patients, respectively, at the vascular level, myointimal thickening, under the electron microscopy, altered organization of myofibrils.
Kautzner J et al/ 2021	VT	**Patients:** 3 patients: 1 with noninchemic cardiomyopathy and two with ICD **Methods:** a post-mortem histological investigation of the myocardium after STAR was performed	**Outcome:** apoptosis of cardiomyocytes in the first 3 months and post-mortem fibrosis as delayed effect **Conclusions:** in 2/3 patients delayed fibrosis was detected after STAR
Rienstra P et al/ 2021	AR	**Objective:** to assess the STAR safety **Methods:** 4 white pigs underwent single-chamber pacemaker implantation. CCTs were acquired and 35-40 Gy were delivered, interrogating the pacemakers. Dmax of the great vessels, oesophagus and chest wall were assessed using one sample t-tests, and compared to known constraints as per RTOG 0623 and AAPM Task Group 101.	**Results:** • cardiac structures: fibrosis in the AV node but no other structural changes at other sites at macroscopic and microscopic study of the hearts. • non-cardiac OaRs : mean Dmax ± SD (p-value) were below the threshold value of known constraints for : chest wall (14.7 ± 3.3 (0.02)), oesophagus (10.7 ± 1.1 (< 0.01)), superior vena cava (3.3 ± 4.1 (=0.05)), right pulmonary artery (16.1 ± 6.4 (< 0.01)), right pulmonary vein (15. 7 ± 5 (< 0.01)), left pulmonary artery (11.1 ± 1.7 (< 0.05)), left pulmonary vein (14.1 ± 2.6 (< 0.01)), inferior vena cava (33.60 ± 1.6 (0), (0)); mean Dmax ± SD (p-value) of the ascending aorta (39.4 ± 16.1 (0.12)) similar dose to the threshold values of normal tissues. **Conclusion:** STAR (35-40 Gy) can be delivered in pig models within the dose limits to the normal tissue (chest wall, esophagus, great vessels).

Legend: AF: atrial fibrillation; AR: arrhythmias; CT: computed tomography; CCT: cArdiac computed tomography; EAM: electroanatomical mapping; ICD: implantable cardioverter defibrillator; MRI: magnetic resonance imaging; RT: radiotherapy; STAR: stereotactic arrhythmia radioablation; VT: ventricular tachycardia

Method: A literature search was conducted on PubMed on 25 January 2022. The search strategy was as follows: ("stereotactic" OR "SBRT" OR "radiosurgery") AND ("arrythmia" OR "tachycardia"). We included only preclinical studies on STAR, published in English, with no time limits.

Results: Sixteen papers were included: 14 animal studies (especially pigs, dogs and rabbits) and 2 articles on explanted hearts undergoing histopatological exam. Main findings of the included papers are summarized in Table 1. The STAR dose ranged between 5 and 55 Gy with photons, and between 70 and 160 Gy with ^{12}C beams. Histopatological exams and electrophysiological tests were performed to assess the efficacy, detecting fibrosis in the irradiated area and interrogating pacemakers if implanted, respectively. The minimum dose to obtain an electrophysiological effect (absence of spontaneous arrhythmias) was 25 Gy. The analyzed studies reported fibrosis in the irradiated substrate, which was found to be dose dependent (>30 Gy) in studies where a range of doses was considered. The observed electrical effect was frequently a deceleration to a cardiac block in AV conduction (threshold dose= 40 Gy). Moreover, according to some studies, radiotherapy seems to increase the levels of connexin 43 (a gap junction protein regulating the cell-to-cell communication in the heart) and enhances intracardiac conductivity. With regard to safety, no adverse events or damage in tissues adjacent to the target were observed, even after high dose treatment with ^{12}C beams.

Conclusions: Current preclinical data confirm the feasibility and safety of STAR and the efficacy of the regimen based on 25 Gy in single session. Large-scale implementation of STAR in the clinical setting will require the standardization of treatment planning and delivery and the evaluation of possible late effects on healthy tissues.

P061

NEOADJUVANT OR DEFINITIVE CHEMORADIOTHERAPY FOR THORACIC ESOPHAGEAL CARCINOMA? THE VALUE OF MODERN IMAGING IN A PERSONALIZED APPROACH

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Aims: As a pathologic complete response (pCR) was reported in ~25% of patients in several studies, definitive chemoradiotherapy (dCR) in thoracic esophageal carcinoma (EC) has been increasingly considered, to avoid complications of surgery. Indeed, savage esophagectomy after dCR showed conflicting results in terms of clinical outcomes and perioperative morbidity. Therefore, there is a growing interest to assess the value of modern imaging for increasing pCR and for driving towards the treatment intents during Chemo-Radiation (CR).

Methods: A narrative review was performed using search criteria string 'neoadjuvant (chemo)radiotherapy' (nCR) AND 'definitive (chemo)radiotherapy' AND

'esophageal' AND 'carcinoma' AND 'Imaging' across PubMed from 2016 to 2021. Studies about imaging for response evaluation during and after CR were included.

Results: After CR, PET-CT could be affected by inflammation due to radiation treatment. Most studies in this context are retrospective and often lack in statistical power. Magnetic resonance imaging (MRI) showed high sensitivity in response assessment, but low specificity. Studies on apparent diffusion coefficient (ADC) showed the potential for prediction of response to treatment in EC patients, but no consensus was detected about specific ADC cut-off values. During CR, at a median of 3 weeks (range 2.4-3.3), 18 F-FDG PET-CT has been employed to predict early responses to CR for EC by using metabolic tumor volume and the maximum of standard uptake value. Besides, in a small cohort of patients, total lesion glycolysis was suggested to be more reliable. MRI has been investigated for prediction of treatment response in EC during nCR, reporting a positive association between an increase in ADC and positive therapy response. Moreover, dynamic contrast–enhanced (DCE)-MRI assesses relative tumor blood volume and vascular permeability, associated with neoangiogenesis and tumor growth. Poorly perfused and hypoxic tumors have been correlated with worse outcomes in EC, due to treatment resistance. Therefore, it's speculable that they could be useful to predict the response to CR.

Conclusions: Currently, a single Imaging cannot predict and evaluate residual disease after CR. This review highlights that a combination of different Imaging modalities pre, during and after CR could be useful to modulate the treatment intent on the individual response trend and to drive in advance and with reliability towards total doses.

P062

IMPACT OF PET/CT SIMULATION ON NEOADJUVANT INTENSITY MODULATED RADIATION THERAPY PLANNING IN LOCALLY ADVANCED RECTAL CANCER (LARC)

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Aims: The aim of this study is to evaluate whether functional imaging with F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET), combined with computed tomography scan (CT) and magnetic resonance imaging (MRI), gives additional information to standard pretreatment evaluation and changes in target definition in rectal cancer patients receiving neoadjuvant chemoradiotherapy (CRT).

Method: From February 2021 to May 2022, 16 patients with locally advanced rectal cancer were enrolled for inclusion in this study to received preoperative concurrent capecitabine and photon IMRT (50.4 Gy in 28 fractions) to the whole pelvis. Standard GTV was delineated using information from clinical examination, CT and MRI (GTV-MRI). A GTV-PET was also defined in the coregistered PET/CT and the target volume delineations were compared for total volume, overlap and mismatch.

Results: The integration with F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) changed the target volume definition in 25% patients: in many cases the GTV-MRI contained the GTV-PET; however, we found that in 31,2% of patients the CTV based on PET extended outside the CTV used in clinical practice. FDG-PET changed the treatment strategy in 3 patients: distant metastases were identified. IMRT and coregistered TC, PET and MRI imaging was significantly associated with increased odds for complete (CR) and partial response (PR): CR= 31.2% and PR: 62.5%.

Conclusions: PET/CT simulation was revealed essential to determine the staging and the consequent treatment strategy. The integration of 18F-FDG PET/CT simulation with pretreatment TC and MRI in IMRT Radiotherapy planning improves delineation of target volumes and odds for complete and partial response. These results are encouraging to considered the integration with PET/TC simulation the standard in radiotherapy planning for LARC.

P063

STEREOTACTIC RE-IRRADIATION IN RECURRENT PROSTATE CANCER USING MRI AND PET/TC FOR TUMOR VOLUME DELINEATION: OUR EXPERIENCE

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Aims: The management of locally Recurrent Prostate Cancer (RPC) after previous post-operative or definitive radiotherapy remains a matter of debade. In recent years, different local approaches have been proposed as a therapeutic option. Curent literature data report the use of Stereotactic Body RT (SBRT) is safe and feasible in RPC. The use of MRI and PET/CT for radiotherapy planning may help to better tumor volume definition because accurate delineation is required for correct treatment. In this report, we present our preliminary experience of re-irradiation using stereotactic body radiotherapy for localized prostate cancer failure.

Method: Between December 2019 and June 2022, 9 patients with RPC (mean age 77.4 years) were treated by SBRT directed to the prostate or bed prostate. 7 patients had recurrences after postoperative radiotherapy, 2 patients had recurrences after radical radiotherapy. All

patients were treated with VMAT-IGRT tecnique linac-based. The prescription dose consisted of 6-7 Gy/fraction to a total dose of 30-35 Gy. A MRI and C-coline or 68Ga-PSMA PET/TC exam was performed both for staging and for treatment planning and in this case images were co-registrared and used for tumor volume definition. The primary outcome is to estimate the efficacy of treatment in terms of time of biochemical recurrence and local control. Secondary outcomes were acute and late genitourinary (GU) and gastrointestinal (GI) toxicities evaluated according to the Common Terminology Criteria for Adverse Events version 5.

Results: After a median follow-up of 11 months (range 1-26), 2 patients (22.2%) experienced biochemical recurrence corresponding to metastatic progression without evidence of local recurrence. Treatment was well tolerated. Acute G2 gastro-intestinal toxicity was reported in only 1 patient and acute G2 genitourinary toxicity in two patients. No late gastro-intestinal and genito-urinary toxicity was observed.

Conclusions: Our preliminary report showed that SBRT re-irradiation could be safe and effective treatment with excellent acute toxicity profile and we reserve further evaluation regarding late toxicity. RMI and PET/TC imaging in radiotherapy planning improves delineation of target volumes redicing the uncertainties and variabilities of radiation treatment.

P064

FLUOROETHYL-L-TYROSINE PET IN GLIOMA RADIOTHERAPY PLANNING: AN ISOTOXIC DOSE PRESCRIPTION APPROACH

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Aims: To use a personalized isotoxic dose prescription (IDP) approach for dose escalation on the FluoroEthyl-l-Tyrosine PET-defined biological tumor volume (BTVFET-PET) in patients with newly diagnosed high grade gliomas (HGG).

Method: We collected data of 31 patients affected by HGG and treated at our Institution between January and December 2021; 7 patients were included in this preliminary study. Simulation CT was coregistered with a CE-3D T1 weighted MRI scan and a FET-PET CT scan, using the deformable registration algorithms of MIM (7.0.6). CTVMR included the area suspected for residual disease in the CE-3D T1 weighted MRI scan (GTVMR) and the operative bed +1.5 cm safety margin, individually adapted to anatomical barriers. PTVMR was generated by adding a 3 mm margin to CTVMR. The BTVFET-PET was defined as the volume within a tumor-to-background ratio cut-off value ≥2.5. Prescribed dose to PTVMR was 60 Gy in 30 fractions. Two planning strategies with VMAT using two arcs in non coplanar geometry were generated for each patient: 1) a plan with homogeneous dose prescription (HDP) on the PTV, and 2) a plan with an inhomogeneous dose (nHDP) prescription where a SIB on the BTVFET-PET was performed. Dose constraints based on QUANTEC review were considered as hard constraints. Following an isotoxic approach, the SIB dose prescription was determined by constraints on OARs, without any limit for the maximum dose into the BTVFET-PET. Plans were automatically generated using the template approach of Monaco 5.12 with radiobiological and multi-criterial cost functions.

Results: There was large variation between BTVFET-PET and GTVMR of the seven patients (median volume: 8.18 ± 17.2 cc *vs* 24.6 ± 13.0 cc, respectively). Dosimetric difference between HDP and nHDP strategies are summarised in Table 1. The OARs dose constraints were met in all plans. Dose to healthy tissues was not significantly different in the two classes of plans.

Conclusions: IDP approach enables safe dose escalation into the BTVFET-PET with a mean prescription dose of 70 Gy in 30 fractions. Prospective studies are needed to confirm whether this promising strategy may improve clinical outcomes of HGG.

Table 1.

Dosimetric data	HDP strategy	nHDP strategy
Average $BTV_{FET\text{-}PET}$ mean dose	62.2 ±0.8 Gy	70.0 ±1.1 Gy
Mean $BTV_{FET\text{-}PET}$ D98%	60.8 ±1.2 Gy	66.1 ±1.1 Gy
Average $BTV_{FET\text{-}PET}$ max dose	64.8 ±0.7 Gy	74.9 ±2.2 Gy
Average PTV mean dose	61.4 ± 0.8 Gy	61.8 ±0.9 Gy

P065

TO EVALUATE VOLUME CHANGES ON COMPUTED TOMOGRAPHY (TC) AND MAGNETIC RESONANCE IMAGING (MRI)-BASED DELINEATION DURING RADIOTHERAPY TREATMENT PLANNING IN PROSTATE CANCER

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Aims: The aim of the present study was to evaluate the impact of magnetic resonance imaging (MRI) on radiotherapy target volume changes in prostate cancer. MRI was used for target delineation and compared with volumetric dimensions acquired from planning computed tomography (CT) scan during treatment planning in patients with prostate cancer.

Method: Patients with localized prostate cancer receiving radical hypofractionated radiotherapy were included in the study (dose prescription: 70.2 Gy, 2.7 Gy/die). Computerized tomography (CT) simulation was done with adequate immobilization, and pelvic MRI was also done at the same time. All patients were asked to follow a strict bowel and bladder protocol. 2.5 mm CT scan slices were taken, and then similar MR images were taken with the immobilization system in the same position. Image registration between planning CT scan and TSE-CS-T2w 3D and T1w-3D pre-treatment MRI was performed. Target delineation (clinical target volume [CTV]) was done on both the image sets separately and their volumes were compared.

Results: From 05.2021 to 05.2022, 33 patients aged 61 to 78 years were included in this study. It has been found that the CT image-based contouring overestimated the CTV as compared to that by MRI images for all patients considered (Figure 1). The mean CTV on CT scan was 93.4 cm^3 (standard deviation [SD]= 39.1), whereas, on MRI images, it was 70.2 cm^3 (SD=33.3). Mean CTV defined by MRI was found to be 37.5% smaller (volume difference of 23.2 cm^3) than that defined by CT scan and this difference is statistically significant (p=0.012). Rectal content and gas issues were more challenging for MRI-only simulation compared to CT-only simulation due to the longer MRI scan time. The results showed that the volume of the rectum detected on CT was greater than that detected on MRI in 54.5% of cases. On average, the difference between the volume of the rectum identified by CT and that identified by MRI was 7.2%.

Conclusions: It can be concluded that MRI is found to be a better modality for CTV delineation, as it gives superior soft-tissue contrast. This fact can be used as an advantage, especially for radical prostatic radiotherapy or boost planning. Hence, the fusion of MRI with CT images together should be used as a routine procedure for radiotherapy treatment planning in prostate cancer.

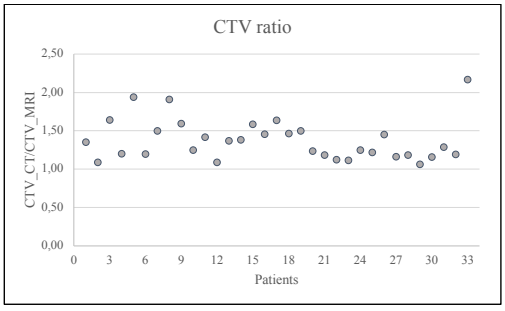

Figure 1. CTV ratio.

P066

PET/CT IN RADIOTHERAPY PLANNING FOR HEAD AND NECK CANCER

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Aims: Aim of this report is to investigate the value of PET/CT fusion in radiotherapy treatment planning for Head and Neck cancer.

Method: 12 patients with Head and Neck cancer, candidated to radical (chemo)radiotherapy using IMRT, received FDG PET/CT-scanner in radiation treatment position. A customized thermoplastic head, neck and shoulders mask were used to immobilize patients. PET/TC images were transferred to the Varian Eclipse planning system and co-registrated with TC scans using an automatic multimodality image registration algorithm. Abnormal areas of fluorodeoxyglucose (FDG) uptake were contoured on PET for the gross tumor volume of primaries (PET-GTVp) and abnormal nodal region of primaries (PET-GTVn), then compared with the same CT gross tumor volumes (TC-GTVp) and abnormal nodal region (TC-GTVn). A statistical analysis was performed to evaluate the correlation of PET and CT volumes.

Result: PET/TC demonstrated the primary in all cases, whereas CT did not find the primary in 1 case. GTVs for the primaries were significantly larger on CT. The average ratio of TC-GTVp/PET-GTVp was 2.7

(range 0.2-22.4), whereas for TC GTVn /PET GTVn was 0.3 (range, 0-3.6). In 3 patients additional areas of disease were seen only in PET. In 3 patients PET/CT led to change of the stage from M0 to M1, leading to change in therapeutic strategies.

Conclusions: PET/CT can increase the accuracy of the staging and defining target volumes for Radiation Therapy fields for Head and Neck cancer.

P067

O-(2-18F-FLUOROETHYL)-L-TYROSINE POSITRON EMISSION TOMOGRAPHY (18F-FET PET) FOR THE STUDY OF BRAIN TUMORS

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Aims: MRI is the standard neuroimaging method used for diagnosis of brain tumors. Amino acid analog PET tracers (11C-methyl-L-methionine (11CMET), O-(2-18F-fluoroethyl)-L-tyrosine (FET) and 3,4-dihydroxy-6-18F-fluoro-L-phenylalanine (FDOPA)) represent an excellent tool to assess the physiopathology of brain cancers, due to the high amino acid selective uptake in tumor tissue and low uptake in normal brain tissue.

Method: At our center we have written a protocol that involves the use of 18F-FET PET in brain tumors and we have chosen two main clinical areas:

- Definition of Biological target volume (BTV).

The metabolic information provided by a PET study can be further utilized to characterize the anatomical gross tumor volume (GTV) by identifying functional subvolumes leading to the definition of a BTV. Some studies reported significant discordance in size and location between contrast enhancement on MRI and FET PET. Amino acid PET tracers can be useful because, as gliomas, metastatic brain tumors overexpress L-amino acid transporter (LAT), independently of the primitive tumor and especially for lesions more than 1 cm.

- Definition of Pseudoprogression, Recurrence and Radionecrosis (RN)

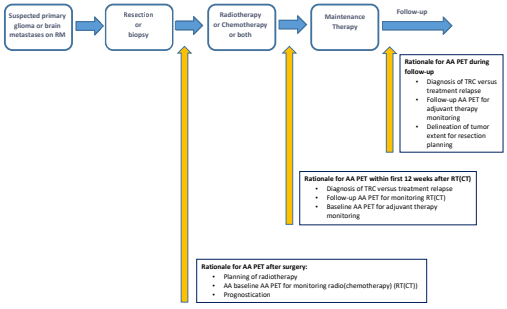
Differentiating treatment related changes (TRC) from disease progression is of critical importance for patients' management and prognosis and it can often be challenging. Pseudoprogression occurs typically within the first 12 weeks after radiotherapy completion while RN typically occurs more than 6 months after radiotherapy and can even occur up to several years later. Differentiating brain tumor recurrence from RN can be challenging during mpMRI follow-up after radiotherapy, both in primary tumors and in brain metastases. According to the RANO/PET working group, amino acids PET tracer should be preferred in this indication.

Results: The main objective of the project is the production of 18F-FET in the radiopharmacy of the Nuclear Medicine Service. Secondary "practical" objectives are (Table 1):

1) Performing 18F-FET PET in the diagnostic of patients with brain tumors and metastases;
2) Use of 18F-FET PET diagnostic information in radiotherapy "simulation";
3) Monitoring therapy.

Conclusions: The ability to better define tumor extent and biology may be used to improve the therapeutic ratio of radiation treatment. Differentiating TRC from disease progression is of crucial importance in clinical practice.

Table 1. Workflow of use of O-(2-18F-fluoroethyl)-L-tyrosine (FET)-PET.



P068

STEREOTACTIC RADIOSURGERY FOR THE TREATMENT OF BRAINSTEM METASTASES: A MULTICENTER RETROSPECTIVE STUDY

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Aim: Brain stem metastases (BSM) is a rare site of occurrence and their management is a challenging issue. Based on the lack of evidences, the optimal radiation treatment of BSM remains controversial. We evaluated the efficacy and toxicity of linear accelerator (linac)-based stereotactic radiosurgery (SRS) and steretotactic radiotherapy (SRT) in the treatment of BMS in a series of patients treated in different centers.

Methods: We conducted a multicentric retrospective study of patients affected by 1-2 BSM from different solid who underwent SRS/SRT. Freedom from local progression (FLP), cancer-specific survival (CSS), overall

survival (OS), and toxicity were evaluated. Moreover, predictive factors of treatment response and survival were evaluated.

Results: Between 2008 and 2021, 105 patients with 111 BMS received SRS or SRT for 1-2 BSM. Median follow-up time was 10 months (range 3-130). One-year FLP rate was 90.4%. At the univariate analysis, tumor volume <0.4 cc and concomitant target therapy were associated with longer FLP, with concomitant target therapy that remained a significant independent predictor [0.058, HR 0.139 (95% CI 0.0182-1.064]. Median OS and CSS were 11 months and 14.6 months, respectively. At multivariate analysis, concomitant target therapy administration was significantly associated with longer OS [HR 0.514 (95%CI 0.302-0.875); p=0.01]. Neurological death occurred in 30.4% of patients, although this was due to BSM progression in only 3 (2.8%) patients.

Conclusion: Brainstem metastases can be safely treated with linac-based SRS with apparent no detrimental effect on survival. When treated with ablative intent, BSM are an uncommon cause of ND. Future prospective trial should answer the question of whether BSM should be excluded a priori from clinical trial.

P069

PATTERN OF RADIATION INDUCED TEMPORAL LOBE NECROSIS AFTER PROTON RADIOTHERAPY FOR SKULL BASE TUMORS AND NTCP MODELS EVALUATION: A MONOCENTRIC RETROSPECTIVE STUDY

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Aims: Radiation induced temporal lobe necrosis (TLN) is a potential complication of radiotherapy for skull base tumors (SBT). The aims of this study were: to analyze the relationship between TLN and dosimetric features in SBT patients treated with pencil beam scanning proton therapy (PT) and to test available normal tissue complication probability (NTCP) models.

Methods: Clinical and dosimetric data of 110 adult consecutive SBT (chordoma and chondrosarcoma) patients treated from September 2011 to July 2020 were retrospectively analyzed. A median dose of 70Gy(RBE) [IQR 70-74Gy(RBE)] was planned and delivered in 35-37 daily fractions. Current treatment planning goal for temporal lobe (TL) was limiting the maximum dose to the hottests 2 cm^3 (D_{2cc}) to 71Gy(RBE). Magnetic Resonance Imaging (MRI) showing TLN at the first occurrence were co-registered with treatment planning images. TLN, according to CTCAE v5.0, was analyzed. TLs dosimetric parameters (Figure 1) were investigated for finding a correlation with the TLN's occurrence and severity and then included in NTCP univariate models. Their classification and predictive performances were evaluated by means of goodness of fit (R^2); Area Under ROC Curve (AUC); accuracy, sensitivity and F-score.

Results: Median follow-up was 36 months (IQR 9-98). Twenty-six (24%) and 14 (13%) patients presented TLN G1 and G2, respectively. No TLN>G2 was recorded. 95% of patients had TLN within 50 months from the end of treatment. Among the dosimetric parameters analyzed, $D_{0.5cc}$, D_{2cc} and D_{Max} better correlate with TLN risk. The corresponding NTCP curves are reported in Figure1. For the G2 TLN models based on $D_{0.5cc}$, D_{2cc} and D_{Max}, R^2 was 0.88, 0.95 and 0.92 whereas AUC was 0.80, 0.82 and 0.79, respectively. Moreover, when considering the TD reproducing experimental TLN G2 occurrence, the D_{2cc}-based TLN model achieved the best predictive performance (accuracy=0.71, sensitivity=0.82, F-score=0.33). Tolerance dose at 2 cm^3 of TL for 5% and 20% probability of developing TLN G2 in 5 years were 62.9Gy(RBE) and 72Gy(RBE), respectively, confirming the validity of the dose constraint used for plan optimization.

Conclusions: Patterns of TLN occurrence in patients with SBT underwent PT were comparable with literature data. High doses to very small TL volumes were the major predictors of TLN. This analysis showed that the TL dose constraint, currently in use in clinical practice, correctly predicted TLN G2 occurrence.

dose to a given percentage of volume	$D_{1\%}$, $D_{2\%}$, $D_{5\%}$, $D_{10\%}$, $D_{15\%}$, $D_{20\%}$, $D_{25\%}$, $D_{30\%}$, $D_{35\%}$, $D_{40\%}$, $D_{45\%}$, $D_{50\%}$, $D_{55\%}$, $D_{60\%}$, $D_{65\%}$, $D_{70\%}$, $D_{75\%}$, $D_{80\%}$, $D_{85\%}$, $D_{90\%}$, $D_{95\%}$, $D_{98\%}$, $D_{99\%}$
dose to a given volume in cc	$D_{0.5cc}$, D_{1cc}, D_{2cc}, D_{5cc}
volume receiving a given dose	V_5, V_{10}, V_{15}, V_{20}, V_{25}, V_{30}, V_{35}, V_{40}, V_{45}, V_{50}, V_{55}, V_{60}, V_{65}, V_{70}, V_{75}
average, maximum and minimum dose	D_{avg}, D_{max}, D_{min}
ROI volume in cc	V_{ROI}
general equivalent uniform dose	gEUD

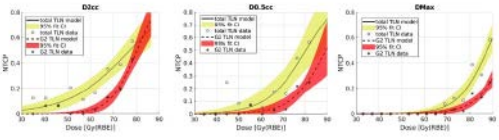

Figure 1 Parameters extracted from DVHs for NTCP model evaluation and univariate analysis of NTCP models (D2cc, D0.5cc, DMax). Shading limits the region within the 95% confidence interval. Solid line-open circles (yellow) TLN G > 0; dashed line-filled circles (red) TLN ≥ G2.

Figure 1.

P070

ELDERLY MENINGIOMAS PATIENTS: MULTIDISCIPLINARY APPROACH AND INDIVIDUALIZATION OF CARE IN THE STEREOTACTIC RADIOTHERAPY ERA

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Aims: To evaluate the stereotactic radiotherapy influence in the multidisciplinary approach of the geriatric patients with diagnosis of meningioma.

Patients and Methods: we retrospectively evaluated all patients with diagnosis of meningioma from July 2007 to May 2022 afferent to our center. Among these, all patients aged> 65 have been selected. All patients had a life expectancy major of 6 months, Charlson Comorbidity Index (CCI) age-weighted with a value ranging from 2 to 8 and Karnofsky Performance Status ≥ 60.

Results: We identified 1088 geriatric patients with meningioma, 591 underwent to surgery and 497 treated with SRS. 363 lesions were in the convexity, 452 of the skull-base, 206 parasagittal, 31 tentorial, 36 patients presented with multiple meningiomatosis or spinal lesions. 43% of patients were over-65. Of these, have been submitted to radical surgery and radiotherapy respectively 17% and 27%. 14% of 1088 patients were over-75 and of these 5% were elected to surgery and 9% were treated with stereotactic radiotherapy. In 30% of 497 patients submitted to SRS, a single fraction was delivered and in 69% a fractionated technique has been chosen. All patients selected to radiotherapy had an age-weighted CCI> 5. No patient died for surgical-related complication. No acute toxicity ≥G3 was detected after SRS treatment.

Conclusions: Our preliminary results show that the stereotactic radiosurgery encourage a higher individualization of the multidisciplinary choices based on age-weighted CCI and KPS in geriatric patients with diagnosis of meningioma.

P071

ENDOCRINE SEQUALAE AFTER CRANIOSPINAL IRRADIATION (CSI) IN LONG-TERM MEDULLOBLASTOMA PATIENTS (PTS)

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Aims: The aim of our study was to describe type and incidence of endocrine sequelae in pts treated with craniospinal irradiation (CSI) with or without high-dose chemotherapy (HCT) for long-term survivors medulloblastoma (MB).

Methods: Study cohort included consecutive pts treated from 1999 to 2018 for MB at our Institution with a minimum follow up of 12 months. After end of treatment all pts underwent oncological and endocrinological surveillance, including periodic blood-based determination of hypothalamus-pituitary-axis and vitamin D. Additional hormone determination could be performed if additional symptoms (*e.g.* slowing of the growth curve, delay in sexual development or alopecia) developed. For each patient, we identified the number of endocrinological deficits, including vitamin D deficiency, at the last follow-up and the timing of their onset.

Results: We evaluated 41 pts, 23 (56%) pts were male. Endocrinological deficits were common, 31 out of 41 pts have shown from single to 4 deficiency: 10 out of 31 pts (33%) developed at least one deficit, 11 (35%) developed 2 deficit, 8 (26%) patients developed 3 deficit, two patients (6%) developed 4 deficits. GH deficiency was the most common alteration (24 pts, 77%) followed by hypothyroidism (18 pts, 58%), both primary (16 pts, 89%) and mixed (4 pts, 25%). Adrenal insufficiency (12 pts, 39%), hypergonadotropic hypogonadism (12 pts, 39%) and hypogonadotropic hypogonadism (1 pts 3%) were less common. Median time to endocrinological deficits onset after end of treatment was 45 months (range 1-186). All patients underwent hormone deficiency replacement therapy. Of a total of 41 patients, 10 (24%) not develop endocrinological toxicity. Table 1 one shows the main treatments characteristics among patients who did

and did not manifest toxicity. Vitamin D deficit was observed in 21 pts (51%), appearing at a median of 60.5 months after the end of CSI. Most pts (19) received vitamin D replacement therapy.

Conclusions: Our study, although limited by a retrospective design and small sample size, shows that endocrinological toxicity are common after CSI for MB, with or without HCT, and can appear long after the end of treatment. This suggests the need for a prolonged and personalized evaluation up until adulthood, especially for pts treated in the pre-pubertal period. Further prospective studies are needed to elucidate the best follow-up strategy and to clarify which factors most determine endocrinological toxicities.

Table 1.

	Overall N 41	Endocrinological Toxicity N 31	No Endocrinological Toxicity N 10
Age at diagnosis (median-years)	6 (range 2-16)	6 (range 3-14)	5 (range 2-16)
Follow-up (median-months)	116 (range 15-250)	116 (range 27-250)	115 (range 15-120)
HCT (%)	22 (54)	18 (58)	4 (40)
HCT timing post-RT (%)	16 (73)	16 (52)	4 (40)
CSI dose (median-Gy)	25.20 (range 23.40-39)	25.20 (range 23.40-39)	24.30 (range 23.40-36)
W-PCF boost (%)	26 (63)	24 (77)	2 (20)
Total dose tumor bed (median-Gy)	55.80 (range 52.40-69)	55.80 (range 52.40-69)	56.40 (range 54-60)

P072

A PROSPECTIVE SINGLE ARM PHASE II STUDY TO EVALUATE SAFETY AND EFFICACY OF SILIBININ IN PATIENTS WITH BRAIN METASTASES TREATED WITH STEREOTACTIC RADIOTHERAPY: PRELIMINARY RESULTS FROM SUSTAIN TRIAL

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Aims: Brain metastases (BMs) account for more than one-half of all intracranial tumors. Survival of patients (pts) with BMs has benefited in recent years from the advent of stereotaxic radiosurgery (SRS); nevertheless, distant brain failure (DBF) remains one of the major concerns. Silibinin or silybin, a natural polyphenolic flavonoid isolated from milk thistle seed extracts, has shown promising antitumor activity both in preclinical and clinical studies, leading to improvement of BMs in pts with progressive non-small cell lung cancer (NSCLC). Therefore, our exploratory study aims to evaluate whether the use of a silibinin-based nutraceutical (SILLBRAIN®, HEALTH4U S.r.l.) can significantly reduce DBF rate at 6 months in pts with first-diagnosed BMs treated with SRS with or without surgery.

Table 1. Baseline characteristics of 23 patients with first-diagnosed BMs treated with SRS with or without surgery. Abbreviations: BM: brain metastases.

Sex, n (%)		
	Male	7
	Female	16
Histology, n (%)		
	NSCLC	10
	Breast	9
	Other	4
Metastases onset, n (%)		
	Synchronous	13
	Metachronous	6
Site of metastases, n (%)		
	Brain	16
	Lung	7
	Bone	5
	Other	19
Previous systemic therapy lines, n (%)		
	No previous lines	7
	1	8
	>1	3
Surgery for Brain metastases, n (%)		
	Yes	6
	No	17
Number of BMs, n (%)		
	1-3	17
	>3	6

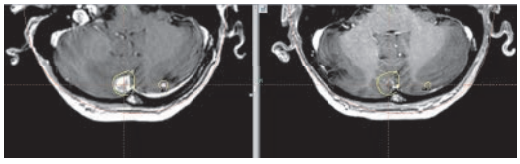

Figure 1. MRI GammaPlan (Leksell GammaPlan®) images during SRS treatment (left) and at a six-month follow-up (right) after complete response.

Method: SUSTAIN is an interventional, prospective, single arm, phase II study. A total of 80 pts treated in our center are planned to be enrolled. Pts receive 2 capsules (cps) of SILLBRAIN® per day for the first month after SRS and 1 cp per day thereafter. Primary endopints are 6-month distant brain failure (DBF) rate and safety; secondary endpoint is 6-month overall survival (OS) rate. Contrast-enhanced magnetic resonance (MRI) of the brain is performed at baseline and every 12 weeks after SRS treatment; radiological response is assessed according to RANO criteria for brain metastases (RANO-BM).

Results: Twenty-three pts had been enrolled at the time of this primary analysis (Table 1). NSCLC and breast cancer were the prevalent histologies (10 and 9 cases respectively). Seven pts were chemotherapy naive at the time of BMs diagnosis; 8 pts had received 1 systemic therapy line and 4 pts had received 2 lines or more. Overall, the number of treated lesions was 53, with a median of 1 lesion (range 1-9). All pts underwent SRS (Figure 1), with a median prescription dose (PD) and a median prescription isodose line (IDL) of 21Gy and 79%, respectively. After a median follow-up of 6 months, 6 pts reported distant intracranial failure according to RANO-BM criteria, with a 6-month DBF rate of 26,1. One pts discontinued SILLBRAIN® assumption due to grade 1 nausea (CTCAE v5.0); no other adverse events were reported.

Conclusions: The use of a silibinin-based nutraceutical has proved to be safe in combination with SRS. Although not markedly improved perhaps due to the limited sample size, DBF was found to be consistent with the literature. Mature results are awaited to confirm our hypotheses.

P073

ATX-101, A PEPTIDE TARGETING PCNA, HAS ANTI-TUMOR EFFICACY ALONE OR IN COMBINATION WITH RADIOTHERAPY IN MURINE MODELS OF HUMAN GLIOBLASTOMA

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Aims: Cell proliferation requires the orchestrated actions of a myriad of proteins regulating DNA replication, DNA repair and damage tolerance, and cell cycle. Proliferating cell nuclear antigen (PCNA) is a master regulator which interacts with multiple proteins functioning in these processes, and this makes PCNA an attractive target in anticancer therapies.

Methods: Here, we investigate the therapeutic efficiency of a cell-penetrating peptide containing the AlkB homolog 2 PCNA-interacting motif (APIM), ATX-101 in a panel of human glioblastoma multiforme (GBM) cell lines and patient-derived glioma-initiating cells (GICs).

Results: ATX-101 show anti-tumor activity in all cell lines used. Their sensitivity to ATX-101 was not related to cellular levels of PCNA, or p53, PTEN, or MGMT status. However, ATX-101 reduced Akt/mTOR and DNA-PKcs signaling, and a correlation between high Akt activation and sensitivity for ATX-101 was found. ATX-101 increased the levels of γH2AX, DNA fragmentation, and apoptosis when combined with radiotherapy (RT). In line with the *in vitro* results, ATX-101 strongly reduced tumor growth in two subcutaneous xenografts and two orthotopic GBM models, both as a single agent and in combination with RT. The ability of ATX-101 to sensitize cells to RT is promising for further development of this compound for use in GBM.

P074

PROTON THERAPY WITH OR WITHOUT CHEMOTHERAPY IN RECURRENT GLIOBLASTOMA

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Aims: To report the results of re-irradiation with proton therapy (PT) with or without chemotherapy (CHT) in difficult-to-treat recurrent glioblastoma (rGBM) patients (pts)

Methods: Between January 2015 and January 2022 fifty-four pts with rGBM were re-irradiated with PT. All pts had been previously treated with Stupp regimen. Twenty-eight (52%) were re-irradiated at first relapse/progression, twenty-six at the second/third one. Fifteen pts (28%) were re-irradiated after partial tumor resection. Median age and Karnofsky performance status at re-irradiation were 54 years and 80%, respectively. Median time between prior radiotherapy and PT was 16 months. Target definition was based on CT, MR, and amino acid PET imaging. Median CTV volume was 54 cc (range, 8-185 cc). All pts received 36 GyRBE in 18 fractions. PT was delivered with or without CHT as follows: 24 (44%) pts (Group 1) received PT only; 7 (13%) pts (Group 2) also received concomitant TMZ (75 mg/m^2/die, 7 days/week); 19 (35%) pts (Group 3) received PT followed by CHT (different regimens/drugs); 4 (8%) pts (Group 4) also received concomitant (as above) and adjuvant TMZ (150-200 mg/m^2/die, 5 days/month). All pts were treated with active pencil beam scanning PT. Side effects were graded according to CTCAE. Health-related quality of life (HRQOL) was assessed by EORTC QLQ-C30 and QLQ-BN20. OS and PFS after re-irradiation were calculated using the Kaplan Meier method

Results: There were no grade 3 or higher acute toxicities. There were no grade 3 or higher late toxicities. During follow-up five pts (9%) developed grade 2 radionecrosis (diagnosed at imaging). The median PFS was 4 months, while 6-month PFS rate was 28%. The median

PFS was 2.5, 7, 5, and 5.5 months for Group 1-2-3-4, respectively. In univariate analysis, secondary GBM (P = 0.02), age < 54 years (P = 0.03), KPS > 80 (P = 0.01), had an effect on PFS. Median OS after PT was 8.5 months. The treatment was consistently associated with improvement or stability in most of the preselected HRQOL domains.

Conclusions: PT re-irradiation of difficult-to-treat rGBM showed to be feasible and safe even with concomitant and adjuvant chemotherapy administration. PT does not negatively effect on HRQOL, but rather it seems to preserve HRQOL until the time of disease progression. PFS and OS rates are promising. PT in association with chemotherapy seems to achieve better results in comparison with re-irradiation only and could deserve further evaluation in a large pts sample.

P075

TEMOZOLOMIDE LONG COURSE HYPOFRACTIONATED RADIOTHERAPY VERSUS STANDARD OF CARE IN THE POST-OPERATIVE SETTING OF GLIOBLASTOMA MULTIFORME: A RETROSPECTIVE MULTICENTRIC ANALYSIS

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Aims: Adjuvant radiation treatment with standard fractionation (SFRT) and short course hypofractionated radiotherapy (hRT) for elderly and/or poorly performing patients in combination with Temozolomide (TMZ) are the standard of care (SC) for patients with newly diagnosed glioblastoma (GBM). Long-course hRT represents a reliable option that has recently demonstrated excellent tolerance and encouraging outcomes in several phase-I studies, even in younger and fit patients. This retrospective multicenter analysis compares safety and effectiveness of SC versus long course hRT on real world large series of GBM patients regardless of age and performance status.

Methods: The study included GBM patients who received SC or long course hRT in the postoperative setting between 2004 and 2021. SC treatment consisted in 60 Gy/30 fractions or 40 Gy/15 fractions according to age, performance status and physician choice. Long-course hRT was delivered into 25 daily fractions with total doses ranging from 60 to 82.5 Gy.

Results: A total of 265 patients were evaluated retrospectively. One hundred twenty-two patients received SC (96 SFRT and 26 short course hRT) and 143 received long course hRT. Seventy-four percent of SC patients were given TMZ, compared to 99% of those who were given long-term hRT. Patients who received SC were somewhat older than those who did not (median, 62 vs 60 years). The intensity modulated radiation treatment (IMRT) technique was used to treat all of the patients. Patients who received SC had a median overall survival of 18 months against 17 months (p=0.11) when compared to those who received long-course hRT. Patients treated with SC had a 2-year OS of 29.3%, whereas patients treated with long course hRT had a 2-year OS of 35.2%. Multivariate Cox regression, which took into account varying total dosages and age, revealed an association between age and overall survival (OS), with OS falling in patients older than 62 years (hazard ratio [HR], 1.82, p<0.001, IC 95%: 1.33-2.50).

Conclusions: Long-course hRT seems to have comparable survival rates as standard fractionation in a large real-world series of GBM patients, but with the benefit of a slight reduction in overall treatment time.

P076

REPEATED HYPERARC RADIOSURGERY FOR RECURRENT INTRACRANIAL METASTASES

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Aims: Stereotactic radiosurgery (SRS) or stereotactic fractionated radiotherapy (SFRT) are effective treatment options in the management of multiple brain metastases (BMs). Furthermore, modern mono-isocentric techniques, like HyperArc, allow the delivery of multiple stereotactic courses, in the event of intracranial failure. Nevertheless, limited data on the efficacy and toxicity have been reported. Aim of this study was to evaluate the effectiveness and safety of multiple HyperArc courses in patients affected by brain metastases (BM) with intracranial progression.

Methods: Between June 2017 and January 2022, we identified a population of 56 patients treated to 702 BM using repeated HyperArc courses. Patients were treated with HyperArc in case of further intracranial progression. Globally, 198 HA courses were administered (range 2-8). Primary tumor was lung 26 (46.5%), breast (32%), melanoma 8 (14%), and other 4 (7.5%). The median GTV volume was 0.1 cc (range 0.08-21.1 cc). BM site was: supratentorial 529 (75%), infratentorial 160 (23%), brainstem 13 (2%). The primary end-point was the overall sur-

vival (OS), secondary end-points were intracranial progression-free survival (iPFS), toxicity, local control (LC), neurological death (ND), and WBRT-free survival

Results: the median OS was 20.8 months (17-36). The 1-, and 2-year OS were 70%, and 46.8%. At the univariate analysis (UVA) BED>51.3Gy and non-melanoma histology were significantly correlated with OS. The median time to iPFS was 4.9 months, and the 1-year iPFS was 15%. Extracranial progression after HA (p=0.05), and cumulative BM volume ≤2.8 cc (per HA course) (p=0.035) were significantly correlated with iPFS and the UVA. Clinical toxicity was represented by headache 4 (7.1%), and radionecrosis 2 (0.28% of treated metastases). One- and 2-year LC was 90% and 79%, respectively. At the UVA BED>70 Gy (p=0.01) and non-melanoma histology (p=0.01) were significant predictor of higher LC. Salvage WBRT was administered in 13 patients (23.2%), and the 2-year WBRT-free survival was 70%. At the last follow-up 12 patients deceased by ND (median time 17.4 months).

Conclusion: Intracranical relapse can be efficaciously and safely treated with repeated HyperArc, with encouraging survival. Neurological death was a relatively rare event in this population. Systemic treatment and extracranial disease should be considered in the decisional workflow. A future study is planned aiming to evaluate neurocognitive function.

P077

DOSIMETRIC IMPACT OF SETUP ERRORS IN SINGLE-ISOCENTER VMAT RADIOSURGERY FOR MULTIPLE BRAIN METASTASES

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Aims: In stereotactic radiosurgery (SRS) and fractionated stereotactic radiosurgery (fSRS) of multiple brain metastases (BM) using single-isocenter volumetric arc therapy (VMAT), intra-fraction positioning errors may affect target coverage. This study aims to investigate geometric and dosimetric accuracy in such applications.

Method: Thirty-two patients (91 BM) treated with single-isocenter coplanar FFF-VMAT technique were analyzed. PTV was defined by a 2 mm isotropic GTV expansion. Pre-treatment setup errors were evaluated with cone-beam CT (CBCT) and corrected with a robotic six degrees-of-freedom couch. Intra-fractional errors for each fraction were measured by post-treatment CBCT and applied to the planning CT. Plans involving translations and rotations (Fx-plan) were re-calculated with Monaco Monte Carlo TPS. Original and Fx-plans were compared in terms of dosimetric parameters, performing the Wilcoxon-Mann-Whitney test (alpha=0.05). The relationships of the BM volume, maximum dimension, distance-to-isocenter, and barycenter shift with the difference in target coverage between the two plans were investigated.

Results: The median post-treatment 3D error was 0.5 mm (0.1–1.5) and the median maximum rotational error was 0.3° (0.1–1.2). The resulting median BM barycenter shift between original and Fx-plans was 0.5 mm (0.1–2.7). The median GTV volume was 0.16 cc (0.01–3.91), while the PTV had a median volume of 0.75 cc (0.12–7.46). Median values of BM maximum dimension and distance-to-isocenter were 9.4 mm (2.9–24.0) and 5.15 cm (0.89–7.52), respectively. The GTV D95% was reduced by >5% in only 2 BM (1 patient), while in 70 lesions (20 patients) a loss of coverage below 1% was observed. The PTV D95% decreased by 1.3% on average, and a dose reduction >1% occurred in 34 PTVs (17 patients). The mean increase of brain V12Gy (SRS) and V20Gy (fSRS) was 0.4% (-0.6–3.6). The dosimetric comparison did not result statistically significant (p>0.05). The difference in target coverage showed a good correlation only with the BM barycenter shift: R2=0.44 and R2=0.50 for GTV and PTV D95% variations, respectively.

Conclusions: Due to the optimal patient setup, as well as the full six degrees-of-freedom corrections, the safety PTV margin, and the fast beam delivery, the dosimetric effects of residual setup and patient motion errors for multiple metastases cases are negligible. These findings warrant a potential reduction in the PTV margin with this treatment technique.

P078

THE "COMBO" RADIOTHERAPY TREATMENT FOR HIGH-RISK GRADE 2 MENINGIOMAS. DOSE ESCALATION AND INITIAL SAFETY AND EFFICACY ANALYSIS

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Aims: The subgroup of "high-risk" WHO grade 2 (hRG2) meningiomas may benefit of adjuvant radiation therapy (RT), but results are still suboptimal with high

rates of local progression. A dose escalation using high-conformal RT techniques needs to be evaluated in terms of efficacy and safety. We report results of a dose-escalation study, named "Combo-RT", combining Intensity Modulated Radiotherapy (IMRT) or Volumetric Arc Therapy (VMAT) with Hypofractionated Stereotactic Radiotherapy (hSRT) boost.

Method: From November 2015 to January 2019, we prospectively enrolled 16 patients with hRG2. Seven patients had subtotal resection (STR) and 9 patients had a recurrent tumor. All patients received Combo-RT: IMRT or VMAT on the surgical bed with a LINAC (Elekta Synergy Platform), and an hSRT boost on residual/recurrent meningioma with a CyberKnife System (Accuray Incorporated, Sunnyvale, California). Toxicity and initial efficacy were evaluated.

Results: The median age was 62 years (range, 31-80 years). For IMRT or VMAT, the median cumulative dose delivered was 46 Gy. For hSRT, the median dose delivered was 15 Gy in 3 fractions at a median isodose line of 77%. Considering an alfa/beta value of 4Gy, the median cumulative BED was 108.75 Gy. The median EQD2 was 72.5 Gy. The whole cohort showed a 3 year-PFS of 75%. Actuarial 3-y PFS for patients with STR was 100%; patients with recurrent tumor had a 3y-PFS of 55.5% (Figure 1a-b). We observed negligible toxicities during and after RT. The majority of patients showed either stable or improved symptoms during long-term follow-up. Salvage treatment for recurrence was an independent predictor of treatment failure (P=0.025).

Conclusions: With the limitation of a small series of patients, our results suggest that a dose escalation for hRG2 meningiomas, using a Combo-RT approach, is safe and particularly effective in the subgroup of patients with STR. Further studies are warranted.

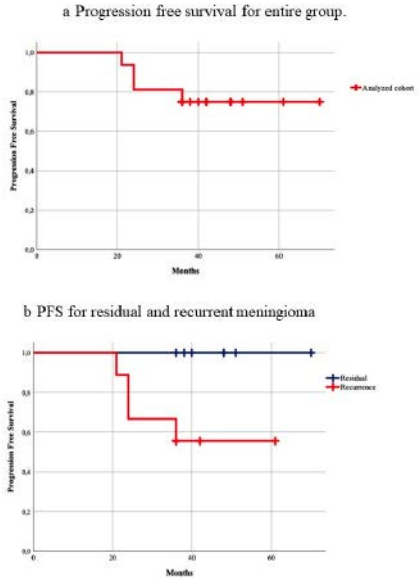

Figure 1.

P079

HIGH RISK OF CENTRAL AND PERIPHERAL HYPOTHYROIDISM AFTER CRANIAL RADIOTERAPY IN A CHORT OF PAEDIATRIC SURVIVORS TREATED FOR BRAIN TUMORS

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Aims: To describe the rate of central (CH) and peripheral (PH) hypothyroidism of pediatric patient with primary brain tumours treated with radiotherapy and/or surgery and chemotherapy.

Table 1.

	Overall, N = 64	Included* Pituitary dose <30.5 N = 15	Included* Pituitary dose ≥30.5, N = 31	p	Excluded* N = 18	p
Male sex (%)	43 (67)	10 (67)	23 (74)	0.855	10 (56)	0.345
Age at diagnosis, Mean (SD)	8.9 (3.9)	8.3 (5.1)	7.7 (2.9)	0.607	11.4 (3.2)	0.001
Age at stop RT, Mean (SD)	10.40 (4.3)	9.7 (4.9)	8.7 (2.9)	0.399	13.8 (4.0)	<0.001
Chemotherapy (%)	56 (88)	14 (93)	30 (97)	0.999	12 (67)	0.006
Surgery (%)	39 (61)	13 (87)	17 (55)	0.073	9 (50)	0.403
Radiotherapy technique (%)						
IMRT	12 (19)	1 (7)	1 (3)	0.999	10 (56)	<0.001
3D	52 (81)	14 (93)	30 (97)		8 (44)	
Type of tumor (%)						
Medulloblastoma	23 (36)	8 (53)	15 (48)		0 (0)	
Germinoma	17 (27)	1 (7)	5 (16)		11 (61)	
Astrocytoma	9 (14)	3 (20)	4 (13)	0.518	2 (11)	<0.001
Glioma	4 (6)	1 (7)	3 (10)		0 (0)	
Ependymoma	3 (5)	2 (13)	1 (3)		0 (0)	
Others	9 (14)	0 (0)	3 (10)		5 (28)	

*Exclusion due to central hypothyroidism present before beginning of RT

Method: We retrospectively analyzed patients from 1999 to 2018, who received radiotherapy for brain tumours, with at least a 2-year-long serological follow-up, to evaluate PH and CH incidence and radiation factors predictive of its onset. CH development was correlate with the site of the primary tumour inside the central nervous system (CNS) (sellar-suprasellar region vs anterior

cranial region vs others). And with type of RT techniques (craniospinal radiotherapy (CSI) versus involved-field radiotherapy (IF-RT)). Dose constraints for CH were determined using the Receiver Operating Characteristic to identify the pituitary mean dose cut-off and the probability of CH over time was assessed with the Cox model. Mean thyroid doses were categorized as 0Gy, < 10Gy and > 10 Gy.

Results: We collected clinical data of 64 patients, of those 18 were excluded due to the presence of CH before RT. 46 pts were analyzed for CH. Table 1 shows the clinical characteristics. 46 (37%) patients developed CH during follow-up: 14 of 17 (82%) patients received CSI, 3 (18%) IF-RT sellar-suprasellar region and anterior cranial region. A median dose higher than 30.5 Gy to the pituitary gland results in a 4-fold increased risk of central hypothyroidism (HR=3.9; 95% CI 1.1, 13.4; p=0.03). Almost 90% of events occurred within 5 years after treatment ended. 29 of 46 (63%) patients did not manifest CH and were in the "other regions". However, 14 of these (48%) underwent CSI. 4 (6%) patients had peripheral damage (which appears later than the central one) and were treated by CSI: 2 patients received mean thyroid doses <10Gy and 2>10Gy.

Conclusions: The highest incidence of hypothyroidism is in the first 5 years. We strongly suggest an endocrine consultation, with serological monitoring of thyroid hormones, for all patients undergoing involved field cranial irradiation, especially if in the anterior encephalic site, sellare-sovrasellar region or if they underwent CSI.

P080

ACTIVE BEAM SCANNING PROTON THERAPY FOR LARGE SKULL BASE MENINGIOMAS: LONG-TERM RESULTS

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Aims: To report long-term results of active beam scanning proton therapy (PT) for large skull base benign meningiomas

Methods: Eighty-two patients (pts) with large skull base meningiomas were treated with PT between April 2015 and December 2021. Median age was 62 years (range, 48-82) while KPS ranged between 60 and 100 (median 90); 60 were female (73%), and 22 were male (27%). Thirty-two pts (39%) had histologically proven World Health Organization (WHO) Grade I tumors. In remaining pts diagnosis was based on the typical imaging appearance of benign meningioma. All patients received PT for residual, progressive or non-operable lesions. Newly diagnosed tumors received total dose of 50 GyRBE (RBE: relative biologic effectiveness) while progressing meningiomas 54 GyRBE. All pts were treated with active beam scanning PT. Treatment planning was based on morphological magnetic resonance imaging and 68-Ga-DOTATOC-PET. Gross tumor volume ranged from 21 to 64 cc. Median follow-up time was 40 months (range, 3-83)

Results: Registered acute side effects according to CTCAE include grade 1 (19%) and grade 2 (8%) skin erythema, grade 1 (5%) and grade 2 (5%) alopecia, grade 1 (40%) fatigue, grade 1 (5%) and grade 2 (10%) conjunctivitis, grade 1 (10%) pain, grade 1 (5%) blurred vision, grade 1 (10%) headache, and grade 2 (5%) skin hyperpigmentation. One pts (1%) experienced grade 3 pain. There were no further grade 3 or higher acute toxicities. Registered late side effects according to CTCAE include grade 1 (2%) and grade 2 (5%) alopecia, grade 1 (21%) fatigue, grade 1 (5%) and grade 2 (5%) headache, grade 1 (6%) dizziness, grade 1 (3%) blurred vision, grade 1 (3%) and grade 2 (6%) pain, grade 1 (2%) dry eye, and grade 1 (5%) skin hyperpigmentation. Two pts (2%) experienced grade 3 pain. Two further pts (2%) experienced grade 3 optic neuropathy. There were no further grade 3 or higher late toxicities. During follow-up one pts (1%) with cavernous sinus meningioma experienced complete obstruction of intracavernous carotid artery with mild transient symptoms that resolved in few days and brain tissue ischemia detected at MRI (grade 2). Before irradiation this pts already had a meningioma-related near-complete obstruction of the intracavernous carotid artery and received a vascular surgery evaluation. Currently, absolute tumor control is 99%. Moreover, relief of symptoms recorded before irradiation occurred in 40% of pts.

Conclusion: PT is safe and effective treatment for pts with large skull base benign meningiomas.

P081

EFFECTIVENESS AND SAFETY OF PROTON THERAPY FOR SKULL-BASE MENINGIOMAS: A MONOCENTRIC EXPERIENCE

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Aims: Meningiomas of the skull base are difficult to surgically access due to the complex structure of the cranial base and close proximity to critical structures such as brainstem and optic pathway. Large complex-shaped skull-base meningiomas (SBM) can be treated with fractionated proton therapy (PT) as exclusive treatment or after surgery (Figure 1). The aim is to report the effectiveness and safety of PT for SBM.

Methods: Between January 2014 and December

2021, 125 patients (68% female, 32% male) with SBM were treated with PT in our centre. Reirradiation cases were excluded from the analysis. Median age was 55 years (IQR 15–87). Seventy-three (58%) patients received PT after surgery as exclusive treatment after relapse/biopsy or as adjuvant treatment: 61 meningiomas were WHO I, 8 were WHO II-III and in 4 patients WHO grade was unknown. No surgery/biopsy was performed in 52 (42%) patients. PT was delivered with a pencil-beam scanning technique, with a median total dose of 55.8 GyRBE (IQR 45–66) and a median dose/fraction of 1.8 GyRBE (IQR 1.8–3). Median GTV and CTV were 18cc (IQR 0–324) and 32cc (IQR 5–324), respectively. Endpoints evaluated included local control (LC), overall survival (OS), progression-free survival (PFS) and toxicity according to CTCAE v5.0.

Results: Median follow-up was 34 months (IQR 3–89). Three (2.6%) patients had a local relapse: 1 WHO I and 2 WHO II-III. Of the 2 documented deaths, none were definitely related to meningioma (OS disease related 100%). No acute toxicity ≥ G3 was reported in all patients treated. Considering only 112 patients with follow-up > 6 months, 2 (2%) patients developed G3 late toxicity (1 hearing impaired and 1 cerebral edema). Furthermore, late toxicity G0, G1 and G2 were reported in 43 (38%), 37 (33%) and 30 (27%) patients, respectively. No G4-G5 late toxicity was reported.

Conclusions: PT can be considered a good treatment option for patients with SBM due to the high rate of LC and minimal side effects. Moreover, PT seems to be an effective and safe treatment also when it is given in progressive and pre-treated diseases. Prospective studies with longer follow-up will be necessary to confirm the role of PT in SBM according to patients and disease characteristics.

Figure 1.

P082

RADIATION INDUCED BRAIN NECROSIS AFTER STEREOTACTIC TREATMENT ON BRAIN METASTASIS: A SINGLE CENTER EXPERIENCE

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Aims: Stereotactic radiosurgery (SRS)/*fractionated stereotactic radiation therapy* (FSRT) are proven effective treatments for brain metastases (BM), but radiation necrosis (RN) is a possible late effect that can affect patient's quality of life and can be difficult to be distinguished from tumor progression. We report the incidence of RN in patients treated by brain SRS/FSRT at our department.

Methods: Patients treated for BM with SRS/FSRT between 2016-2021 with clinical and *Magnetic Resonance Imaging* (MRI) follow-up (FUP) availability of at least 6 months, have been included in this analysis. RN was scored according to the *CTCAE* 5.0. Clinical (smoking status, immuno- or target-therapy, steroids use during RT, previous surgery, whole brain or focal RT), anatomical (*GTV* volume, location) and dosimetric (*BED2* corrected brain minus GTV *Dmax* and *Vx* across 2 Gy increments of dose) factors were collected; *univariate* and *ROC* analysis were performed.

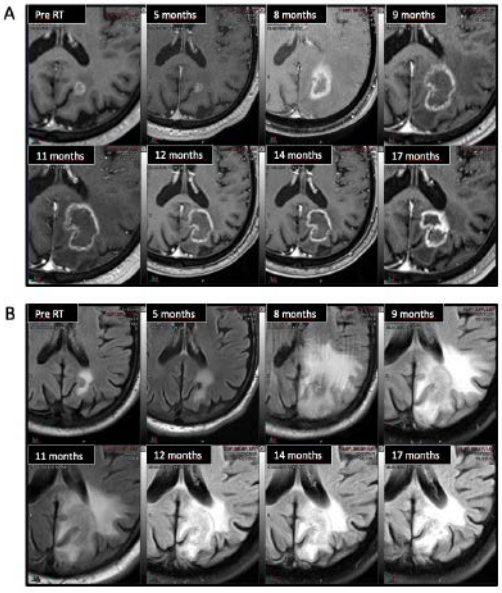

Figure 1. Serial axial *T1*- **(A)** and *T2-weighted* **(B)** MRI of a 74y/o patient with 17 months of clinical and radiological FUP. GTV volume was 0.75cc. Radiological stabilization of G2 RN, edema and neurological deficits have been obtained after 9 months of steroids dependence.

Figure 1.

Results: Forty-three patients with 113 BM met the inclusion criteria. Median clinical and radiological FUP time is 11,5 (6-58) months. G1-2 RN occurred in 11 patients (25%) and 17 lesions (15%), with a median time to onset of 6 (3-46) months. G2 patients noted to have neurological deficits received steroids, and 56% improved or stabilized with treatment, although for 40% of them a phase of 5-16 months of steroids dependence has been faced (Figure 1); for others, the event is still ongoing (33%), or it is unknown (11%). No one required surgical decompression (G3). At univariate analysis, only *GTV* volume resulted significantly ($p<0.05$) related to RN; previous surgery showed a trend towards significance ($p=0.06$). Median GTV volume was 0,23 (0.02-14.85) cc for the G0 RN, and 0.85 (0.2-64.97) cc for the G1-2 RN brain metastases, respectively. Cut-off value of 0.23cc *GTV* volume was found by ROC analysis: G1-2 events occurred in the 25% of BM with *GTV* volume $\geq$ 0.23cc.

Conclusions: The rate of RN incidence that we observed is consistent with that reported in the literature. Diagnosis and treatment remain a challenge, but in our experience, with prompt recognition and medical therapy, radiological and clinical stabilization is obtained in most cases. However, further follow-up is warranted. Risk-benefit ratio evaluation and particular radiological/clinical attention could be required for brain metastasis with a volume of 0.23 cc or more.

P083

SUCCESSFUL PREGNANCIES AFTER HELICAL TOMOTHERAPY CRANIOSPINAL IRRADIATION FOR ADULT MEDULLOBLASTOMA

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Aims: Retrospective study to analyze fertility outcomes in adult medulloblastoma (MB) pts of childbearing age treated with helical Tomotherapy craniospinal irradiation (HT-CSI).

Method: From 2006 to 2021, 12 women of childbearing age (range 20-36 years, median 31) with MB underwent HT-CSI. The prescribed dose was 32.4 Gy (1.8 Gy/fr) for non-metastatic pts, and 36 Gy (1.8 Gy/fr) for metastatic pts, with a boost to the tumor bed and metastases. Administered chemotherapy (CT), performed fertility preservation techniques, menstrual activity, anti-Müllerian hormone (AMH) levels, and doses to the ovaries were recorded. Successful pregnancies resulting in live births after HT-CSI were examined.

Results: At their last fup, all women were alive with a median fup of 4.6 years (range 0.8-10.4). A 31-year-old patient reported a 2-year history of secondary amenorrhea when diagnosed with MB and was excluded. Eight out of the remaining 11 pts were alive with NED with a median fup of 4.6 years (range 1.7-10.4) and were included in the analysis for fertility outcomes. Six non-metastatic pts received 32.4 Gy/18 fr HT-CSI; a subsequent whole spinal boost of 3.6 Gy/2 fr was delivered to a platinum unsuitable patient; 2 metastatic pts received 36 Gy/20 fr HT-CSI, with one receiving a simultaneous integrated boost up to 45 Gy (2.25 Gy/fr) to the cauda equina region. Platinum/etoposide adjuvant CT was administered to 6 pts, together with gonadotropin-releasing hormone agonist; 2 had no CT. Two pts underwent ovarian tissue cryopreservation prior to HT-CSI. Before starting RT, 5 pts had regular menstrual cycles, 2 were taking oral contraceptives, and 1 reported postpartum amenorrhea (4-month-old baby). Pre-RT AMH level was available for 3 pts, resulting <0.1 ng/ml for the postpartum amenorrheic woman (36 years old), and within normal range for the 2 women using oral contraceptives. Data on menstrual activity after oncological treatments were available for 6 pts: 4 recovered regular cycles after 0.7-4 years, while 2 still had irregular cycles at their last fup (at 10.1 and 2.5 years after therapy completion). Maximum dose to the ovaries: 3.4-26.5 Gy. Two women tried to conceive after successful MB treatment, became spontaneously pregnant, and gave birth to full-term healthy children.

Conclusions: In this retrospective study of adult MB women of childbearing age, HT-CSI has not precluded 2 long-term survivors from becoming spontaneously pregnant and giving birth to healthy children.

P084

INTRA-FRACTION ERROR ANALYSIS OF HOME-MADE MOUTH-BITE THERMOPLASTIC MASKS IN LINAC-BASED SRS FOR BRAIN METASTASES

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Aims: This study aims to evaluate the intra-fraction accuracy of stereotactic linac-based radiosurgery (SRS) for brain metastases (BM) using a frameless homemade mouth-bite thermoplastic mask in combination with cone-beam computed tomography (CBCT) and six-degrees of freedom (6-DOF) couchtop.

Method: A frameless approach using a homemade mouth-bite thermoplastic mask (Figure 1) was implemented during Covid-19 pandemic emergency period to offer BM SRS under conditions of limited mobility. All patients were treated at a single institution with single-isocenter coplanar 6 MV flattening filter free (FFF) volu-

metric modulated arc therapy (VMAT) radiosurgery, with a 2 mm isotropic expansion from the gross tumor volume (GTV) to the planning target volume (PTV). Before treatment delivery, patients underwent a low-dose CBCT to check position accuracy. Through image co-registration, translational (x, y, z) and rotational errors (pitch, roll, and yaw) were determined and validated by experienced radiation oncologists. The 6-DOF couchtop was used to automatically relocate the patient with sub-millimetric precision. Immediately after irradiation, patients underwent a second CBCT to evaluate the intra-fraction motion, and data were collected and analysed.

Results: From February 2020 to May 2022, 50 patients (88 lesions) received BM SRS (14-21 Gy). The whole procedure, from the pre-treatment CBCT scan to the end of irradiation and subsequent CBCT, required a median time of 11 minutes [8-19]. Mean translational error was 0.1 mm ± 0.4 mm [-1.0; 1.4] in lateral direction, and 0.0 mm ± 0.4 mm [-1.4; 1.1] in longitudinal direction. A 2.2 mm maximum shift was recorded on the vertical axis, although the mean translation error was 0.0 mm ± 0.4 mm. Pitch, roll and yaw registered a mean value of 0.0° ± 0.4° [-1.3°; 0.7°], 0.0° ± 0.2° [-0.8°; 0.6°], and 0.0° ± 0.3° [-0.9°; 0.9°], respectively.

Conclusions: This study demonstrates that homemade mouth-bite thermoplastic masks provide a steady patient fixation and, combined with CBCT, 6-DOF couchtop, and fast FFF coplanar treatment delivery allow minimal intra-fraction uncertainties in BM SRS. These results, coupled with the study of the dosimetric impact of residual rotational and translational errors, might lead to a reduction of the PTV margin in this setting.

Homemade mouth-bite thermoplastic mask

Figure 1.

P085

VALIDATION OF LEXICOGRAPHIC OPTIMIZATION-BASED PLANNING FOR BRAIN METASTASIS RADIOSURGERY WITH COPLANAR ARCS

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Aim: In this study, a not yet commercially available fully-automated lexicographic optimization planning was validated for intracranial stereotactic radiosurgery (SRS) with coplanar arcs.

Method: Twenty-one single-lesion SRS plans (21 Gy/1 fx) delivered between November 2019 and December 2021 were retrospectively selected and automatically re-planned. An a-priori assigned priority list was used to define the automatic multi-criterial optimization: 4 patient sets were necessary to achieve a robust request list. All plans were re-optimized with 2 coplanar 140°-arcs and calculated with the Monte Carlo. The main criterion for planning approval was a brain V_{12Gy}<10 cm^3. A target coverage as high as possible was requested, with at least 80% of the prescription dose covering 99% of the PTV. The only allowed further manual intervention after automatic planning was the dose normalization. Manual plans (MP) and automatic plans (AP) were compared in terms of dose-volume constraints and monitor units (MUs). Statistical significance was assessed by performing the Wilcoxon-Mann-Whitney test (alpha=0.05). Plan deliverability was verified by pre-treatment QA.

Results: The 21 AP re-planning took only 5 working days, significantly reducing the planning time from about one working day for one MP to about 2 hours for one AP. The median $D_{98\%}$ of GTV and PTV for MP and AP was 20.4 Gy [18.5-21.6] and 18.1 Gy [16.8-19.9], and 21.1 Gy [19.2-21.7] and 19.1 Gy [17.6-19.4], respectively. This coverage increase was statistically significant ($p<0.03$). A significant improvement in PTV Paddick's conformity index has been registered: 0.3[0.0-0.6] for MP and 0.5[0.3-0.9] for AP with a $p<0.001$. The brain V_{12Gy} was 7.3 cm^3[4.4-12.7] and 7.6 cm^3[4.2-13.3] for MP and AP, respectively ($p>0.05$). Other organs at risk were never significantly interested by clinically relevant doses. These results were obtained with a lower median number of MU (-11.6%) even if this difference was not statistically significant and plans registered a comparable gamma analysis (local 2%/2mm).

Conclusions: In AP the target coverage was significantly increased, reducing the MU number and preserving the plan deliverability. The validation showed the novel autoplanning capability to generate high-quality

clinically acceptable and deliverable plans according to institutional-specific protocols: the clinical workflow requests will be answered in a shorter planning time producing plans with a shorter delivery time.

P086

OLD AND NEW SYSTEMIC IMMUNE-INFLAMMATION INDEXES ARE ASSOCIATED WITH OVERALL SURVIVAL OF GLIOBLASTOMA PATIENTS TREATED WITH RADIO-CHEMOTHERAPY

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Aims: Systemic immunity and inflammation indexes (SI) derived from blood cells have gained increasing attention in clinical oncology as potential biomarkers that are associated with survival.

Methods: We tested 12 different SI using blood tests from patients with isocitrate dehydrogenase 1 and 2 wild-type glioblastomas, treated with radio-chemotherapy. The primary endpoint was their overall survival.

Results: A total of 77 patients, comprising 43 males and 34 females, with a median age of 64 years (age range 26–84), who were treated between October 2010 and July 2020, were included in the present analysis (approved by a local ethics committee). In the univariate Cox regression analysis, all the indexes except two showed a statistically significant impact on OS. In the multivariate Cox regression analysis, neutrophil x platelet x leukocyte/(lymphocyte x monocyte) (NPW/LM) and neutrophil x platelet x monocyte/lymphocyte (NPM/L) maintained their statistically significant impact value.

Conclusions: This univariate analysis confirms the potential of systemic inflammation indexes in patients with glioblastoma, while the multivariate analysis verifies the prognostic value of NPW/LM and NPM/L.

P087

PROGNOSTIC FACTORS IN OLDER GLIOBLASTOMA PATIENTS: A MONOCENTRIC EXPERIENCE

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Aims: Older Glioblastoma (GBM) patients often show limited response to treatments and an inherently poor outcome. This is a monocentric retrospective analysis to evaluate clinical features, treatment choices, prognostic factors affecting progression free (PFS) and overall survival (OS) in a single cohort of older GBM patients.

Method: We included patients ≥ 70-year-old. All patients had histological confirmation of GBM, as per WHO CNS5 2021 (IDH1 or IDH2 wild type), with MGMT methylation status assessed. All patients underwent resection or stereotactic biopsy, after which they may received radiotherapy (RT) with or without Temozolomide (TMZ), exclusive TMZ or Best Supportive Care. Karnofsky Performance Scale (KPS) was used to evaluate clinical condition, RANO criteria for radiological assessment.

Results: From Jan 2019 to Nov 2021 66 patients (pts) were treated in our Institution. Median age was 75 (70-85) and median KPS 80% (40-100%). Twenty patients (30%) underwent stereotactic biopsy and 46 (70%) a complete resection. 13 pts presented an unmethylated MGMT status, while 53 had a methylated MGMT status (MGMT 5-25%: 22 pts; 26-50%: 17 pts; > 50%: 5 pts). Sixteen patients didn't receive any oncological treatment, while only 4 pts were treated with exclusive Temozolomide. In the 46 pts treated with RT, the most frequent schedule was 40 Gy in 15 fractions (30 pts), 7 pts received 60 Gy in 30 fr, 9 pts received other hypofractionated schedules. Four pts didn't complete their treatment due to worsening clinical conditions. In 29 pts TMZ was administered both in a concomitant and sequential fashion. At the time of analysis median OS is 6 months (21 days - 39 months) with a median PFS of 4.5 months (8 days - 39 months), with 10 pts alive. At the time of progression, 53 pts didn't receive any further treatments, only 2 pts had new surgery and 2 pts underwent reirradiation, while 9 pts began a II line treatment (Fotemustine: 5 pts; Regorafenib: 4 pts). Complete resection, baseline KPS score, radiotherapy and the possibility to assume a II line treatment for progressive disease were significant prognostic factors in the univariate analysis for OS; but only KPS (p=0,0358) and RT (p=0,0001) were a significant independent OS predictor

in the multivariate analysis. In our cohort, the MGMT methylation status had no impact on OS.

Conclusions: In older patients good clinical status is the major prognosticator for OS and a simple tool to aid the physician in the decision making process.

P088

REGORAFENIB & RE-IRRADIATION: ANALISIS OF CLINICAL OUTCOMES AND TOXICITIES IN PATIENTS WITH RECURRENT GLIOBLASTOMA

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Aims: Glioblastoma is the most common and aggressive primary brain tumor in adults. The aggressiveness and poor prognosis related to this disease join to the limited available treatment options. The current standard of care involves surgical resection followed by concomitant radiotherapy and chemotherapy. At recurrence, no standard treatment exists and there are no guidelines to facilitate decisions in the recurrent setting. Available options include re-operation, re-irradiation, systemic therapy, alone or in combination. In recent years, immunotherapy strategies have revolutionized the treatment of many cancers, increasing the hope for GBM therapy. Regorafenib (Stivarga) is an inhibitor of several kinases involved in the mechanisms that regulate neoangiogenesis processes, through the inhibition vascular endothelial growth factor (VEGF) receptors and the modifications of the tumor microenvironment; specifically, Regorafenib binds and stabilizes PSAT1 (phosphoserine aminotransferase 1). The dual regulatory mechanism underlying PSAT1-induced autophagy arrest accounts for the superior anti-GBM effect of Regorafenib compared with Temozolomide.

Methods: 15 patients with documented disease progression after surgery followed by RT and TMZ were assigned to receive regorafenib (REG) 160 mg once daily for the first 3 weeks of each 4-week cycle. All patients received prior radiation therapy (RT) to a median dose of 60 Gy (range 40.05 -60). Median time to retreatment after prior RT was 16 months (range 14-33). Tumor volumes ranged from 81.7 cm^3 to 422.4 cm^3 (CTV) and from 112.7 cm^3 to 422.4 cm^3 (PTV). 3 patients (20%) received concomitant reirradiation with a radiation dose of 37.5 Gy in 15 fractions of 2.5 Gy.

Results: The median follow-up was 9.5 months (range 5-22). The overall survival and the progression-free survival rates were 53,8 %, and 46,6 % respectively at 2 years. In 53% the symptoms were stable. Only one patient developed late toxicity: acute pancreatitis (Grade I) regressed on interruption of Regorafenib. No other neurological deficits occurred during follow-up. At last follow up 60% of patients were alive.

Conclusion: We report our experience with Regorafenib, administered in patients with rapid progression after the end of postoperative radio chemotherapy treatment. Regorafenib might be a new potential treatment option for recurrent glioblastoma: it was well tolerated also in cases of combined treatment with reirradiation and appeared effective. Other studies will be necessary to evaluate and confirm the role of Regorafenib in glioblastoma patients and the potential effectiveness of the combined therapeutic strategy: Regorafenib-reirradiation.

P089

LINAC-BASED VMAT ABLATIVE RADIOTHERAPY OF BRAIN METASTASES (BM) WITH A NON-COPLANAR MONO-ISOCENTER TECHNIQUE (HYPERARC (HA)): A SINGLE CENTER EXPERIENCE

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*Aims:*We report toxicity and outcome data of our series of patients (pts) treated with HA technique for single or multiple BMs.

Method: We retrospectively reviewed data of pts with BMs treated with HA at our Department. Response of treated lesions or the onset of new ones, overall survival (OS) and toxicity were evaluated.

Results: 76 pts (43 males, 33 females), with a total of 196 BM, treated at our Department from March 2019 to April 2022, were reviewed. 66 pts had a single treatment, 9 a second HA treatment (Tx), and 1 a third. Of these 10 pts, 9 had an onset of new BM with stable dimensions or a reduction of the treated ones; 1 pt had an increase of the treated BM and an onset of new ones. Overall a total of 87 Tx courses were performed. Median age at diagnosis was 64 years (range 24 - 83). A single BM was treated in 39 Tx courses, while multiple BM were simultaneously irradiated in 48. In 5 Tx, the surgical bed was one of the targets. The average diameter of the greatest lesion in each Tx was 2 cm, (range 0.2 - 9). Primary tumour histology was lung in 30 pts, breast in 15, melanoma in 8, kidney in 6, colon in 5, pancreas in 3, prostate in 2, cardias in 1, thymic carcinoma in 1, testis germinoma in 1, parotid in 1, base of tongue in 1, endometrium in 1, oesophagus in 1. The GTV encompassed the macroscopic contrast enhancing lesion on T1-MRI and was assumed to be equal to the CTV. The PTV was obtained from the GTV plus an isotropic margin of 2 mm. Dose prescription was 27 Gy in 3 fractions or 21 Gy in a single fraction, according to lesions size and brain localization. A 21-Gy sin-

gle-fraction treatment was delivered in 23 Tx courses. In this group of pts, the average diameter of the greatest lesion was 1 cm (range 0.2-3.3). 27 Gy in 3 fractions were delivered in 64 Tx courses. In this group of pts, the average diameter of the greatest lesion was 2.4 cm (range 0.3-9). All 5 surgical cavities were treated with 27 Gy in 3 fractions. After a median follow-up of 7 months (range 1-36), treated lesions dimensions were stable or reduced in 82 out of 87 Tx courses; instead, an increase in the size of treated lesion was observed in 5 out of 87. In the whole series, median OS was 8 months (range 1 - 39). No pts developed G2 or G3 toxicities.

Conclusions: HA treatment was well tolerated in our series, even when repeated once or twice. Local control data were excellent, even when HA is delivered on the surgical bed after BM excision.

P090

POTENTIAL ROLE OF PRE-RADIOTHERAPY MRI FOR TARGET DELINEATION IN HIGH-GRADE GLIOMAS: A MULTICENTER RETRO-PROSPECTIVE COHORT STUDY

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Aims: The aim of the study was to retrospectively confirm that RT planned on pre-RT MRI might allow to spare more normal tissue without decreasing local tumor control, in order to prospectively evaluate the best standard and advanced MRI and metabolic imaging sequences for clinical tumor volume (CTV) adaptation.

Method: We analyzed a retrospective cohort of patients with HGG treated from 2017 to 2020 at our Institutes. All patients had a diagnostic MRI and an immediately post—surgery or pre-RT MRI. Patients were divided into two groups: in group A target volumes were contoured on diagnostic and post-surgery T2/FLAIR MRI, while in group B on pre-RT MRI. We analyzed gross tumor volume (GTV) and CTV volume, and the percentage increase between them. Moreover, we compared the two groups in terms of clinical-pathological characteristics and progression-free survival (PFS) and overall survival (OS).

Results: In retrospective cohort we analyzed 54 patients (25 group A, 29 group B). The median age of patients was 61 years (IQR 17,75), 93% had an ECOG PS of 0 or 1, 51 were symptomatic at diagnosis. Patients in group B had more frequently MGMT methylation (59 % vs. 28%, p=0.01) while less frequently frontal lobe involvement (60% *vs* 24%, p=0.01). The median percentage increase between GTV and CTV was higher in group A than B: 431% (range 62%-7335%) vs 385% (range 53%-3174%), respectively. No significant difference in the pattern of relapse was observed, since >90% of disease recurrences were in-field in both groups. Median PFS and OS of the overall population were 9.5 months (95% CI 7 - 12) and 18.5 months (95% CI 16 - 24), respectively. Patients in group B had a significant better PFS as compared to those in group A (p=0.03), but similar OS. Nevertheless, imbalance in MGMT methylation status between the two groups was a major driver for PFS. Overall, 37 out of 51 patients had improvement in neurological symptoms (p<0.001), with no difference between the two groups (p=0.54).

Conclusions: Our data suggest that CTV adaptation to pre-RT RMI T2/FLAIR may allow to reduce RT volume, without affect symptoms relieving and disease control. Results from the prospective study will help identifying the best adaptation of CTV guided by T2/FLAIR, advanced MRI sequences, in order to optimize efficacy and safety of treatment planning.

P091

ROLE OF MAGNETIC RESONANCE IN CLINICAL DECISION MAKINGIN PATIENT WITH HIGH GRADE GLIOMA INDERGOING POSTOPERATIVE RADIOTHERAPY

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Aims: Magnetic resonance (MRI) has a central role in follow up of high-grade glioma patients undergoing postoperative radio chemotherapy (RT-CT). The introduction of RANO criteria has changed our clinical decision process because of the potential onset of pseudoprogression inside the radiotherapy field within the first 6 months following RT-CT. The aim of this study is to evaluate the role and the best timing of MRI following RT-CT in patients diagnosed with high-grade glioma.

Methods: We retrospectively evaluate patients with a pathological diagnosis of high-grade glioma, treated between May 2013 and July 2020. All patients received RT-CT (30 Gy in 2 Gy fraction and Temozolomide (TMZ) 75 mg/mq daily) on the surgical bed (or the residual disease) plus 2 cm of margin and a sequential TMZ (150 mg/mq for the first cycle, then 200 mg/mq) until toxicity, disease progression or up to 12 cycles. Clinical examination and MRI were planned 4-6 week after RT-CT and then every 3 months. We recorded radiological evaluations, symptoms related to disease progression and the change of therapeutic strategy. In case of disease recurrence inside the treatment field, RANO criteria were adopted to differentiate actual progression from a pseudoprogression. New lesions grown up outside the treatment field were considered as distant recurrence. Patients received salvage therapies or best supportive care in case of disease recurrence.

Results: We evaluate 149 patients, 123 patients had glioblastoma (GBM) and 26 had glioma WHO grade III. 69 patients underwent gross total resection (GTR), 82 underwent subtotal resection (STR) or biopsy only. Median follow-up was 33 months, median overall survival (OS) was 23.4 months, median progression-free survival (PFS) was 8.5 months. 2 out of 122 (1.6%), 5 out of 106 (4.7%) and 8 out of 92 (8.6%) asymptomatic patients received the diagnosis of disease recurrence at the time of the first, second and third MRI, respectively. Otherwise, 16 out of 27 (59.2%), 16 out of 24 (66.6%) and 13 out of 16 (82.2%) symptomatic patients changed their therapy after the first, second and third MRI, respectively. Among patients that experienced radiological signs of distant progression, 10 out of 14 were symptomatic and changed their therapy.

Conclusions: The impact of the MRI performed during follow up of high grade glioma patients seems limited to the symptomatic ones while to the clinical decision-making of asymptomatic patients is limited and often confounding.

P092

OUTCOMES OF LARGE VOLUME MENGINIOMAS TREATED WITH HELICAL IMRT/V-MAT WITH LONG FOLLOW-UP: MONOISTITUTIONAL EXPERIENCE

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Purpose: We present the outcomes of large meningiomas treated with conventionally fractionated radiotherapy with HelicalTomoTherapy (Accuray Sunnyvale CA) (TT) and RapidArc (Variant Palo Alto CA) (RA) in our Institution.

Table 1. Acute and late toxicity.

	G0	G1	G2	G3	G4
ACUTE	ACUTE TOXICITY (52pts)				
Nausea	42 (80.8%)	10 (19.2%)	0 (0%)	0 (0%)	0 (0%)
Headache	44 (84.6%)	7 (13.5%)	1 (1.9%)	0 (0%)	0 (0%)
Neurological Deficit	44 (84.6%)	6 (11.5%)	1 (1.9%)	1 (1.9%)	0 (0%)
Others	28 (53.8%)	18 (34.6%)	6 (11.5%)	0 (0%)	0 (0%)
	LATE TOXICITY (48pts)				
Headache	46 (95.8%)	1 (2.1%)	1 (2.1%)	0 (0%)	0 (0%)
Neurological Deficit	27 (56.3%)	10 (20.8%)	6 (12.5%)	4 (8.3%)	1 (2.1%)
Others	30 (62.5%)	8 (16.7%)	10 (20.8%)	0 (0%)	0 (0%)

Materials and Methods: The records of intracranial meningioma patients treated between 01/2015 and 12/2017, in order to have a 5-year follow up, were analyzed. Median age of the 52 patients identified was 61.3 (32.3 – 84.2) years, 65% were female and 35% male. Eighteen patients had radiological diagnosis only. Of the 34 patients operated on 17 were grading (G) 1 (WHO 2021), 15 G2 and 2 G3. Most common symptoms at diagnosis were headache (27%) and visual deficits (38%). Intracranial localization was: skull-base (SKB) for 34 patients (65%), convexity for 13 (25%), posterior cranial fossa (PCF) for 4 (8%), orbital for 1 (2%). Forty-three patients were treated with TT, 9 with RA. Median prescribed dose was 50.4 (46.8-60)Gy in 28 (25-30) fractions, with a median dose/fraction of 1.8Gy. Pre-treatment PS-ECOG was 0 in 37%, 1 in 50% and 2 in 13% of patients.

Results: Median follow-up was 56 (2.9 – 89.2) months. Median planning-target-volume (PTV) was 104.8 (24.4 – 367.01) cc. Half of patients did not require corticosteroid therapy during treatment. Acute and late toxicity were evaluated with CTCAE v5.0 and reported in

table 1. Late toxicity was evaluated in 48 out of 52 patients. During the follow up period hypopituitarism was presented by 12.5% of pts, 18.8% presented a worsening of visual deficits (only 1 G4 blindness), while 10.4% registered an improvement. Worsening of hearing was observed in 12.5% of pts. Seven out of 52 patients (13.5%) presented local relapse, disease-free-survival (DFS) was 54.94 (2.12 – 89.19) months. Five patients died from other reasons during the follow up period.

Conclusion: Good local control and overall survival with low acute and acceptable late toxicity was obtained with Helical IMRT/V-MAT in patients with large volume meningiomas with conventionally fractionated radiotherapy.

P093

STEREOTACTIC RADIATION THERAPY FOR BRAIN METASTASES: A SINGLE CENTER EXPERIENCE

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Aims: To retrospectively review the outcome of *stereotactic radiosurgery* (SRS)/ fractionated stereotactic radiation therapy (FSRT) for brain metastasis (BM) in patients treated at our department.

Methods: Patients treated with SRS/FSRT for brain metastases (BM) for which follow up (FUP) information were available have been included. Tumor response was evaluated by the *RANO* criteria. Survival outcomes – local failure free survival (LFFS), brain progression free survival (BPFS), progression free survival (PFS), overall survival from RT (OSRT) and from diagnosis (OS)- were estimated with the *Kaplan-Meier* method; *univariate* analysis was performed to evaluate possibly related factors.

Results: Ninety-eight patients and 206 BM were treated since 2016. With a median FUP of 9 months (1-65), 79 patients (47% males, 53% females) were included in this analysis. Median age at diagnosis was 57 (25-74) years: 66% have been diagnosed at local/locally advanced stage, 34% at metastatic. Median time from diagnosis to BM was 6 (0-124) months. A total of 175 BM arising from different primaries (26% breast, 23% lung, 11% melanoma, 10% colorectal, 30% others) were treated: SRS amounts to 49%, FSRT to 51%. The most used schedule was 18 Gy (50%) for SRS and 27/9 Gy (41%) for FSRT. Median *BED20* was 50,4 (34,3-81,6) Gy. Median age and KPS at time of RT were 61 (38-82) years and 90 (40-100)%, respectively. Forty-two percent treatments were performed with stable extracranial disease, 58% with active or new diagnosis. The crude local control is 88%, with no clinical or treatment factors significantly related to local failures. Half of patients underwent whole brain or further SRS/FSRT for brain progression; 9,5% underwent reirradiation. Estimated median BPFS, PFS, OSRT and OS are 9, 6, 18 and 68 months, respectively. Estimated LFFS rates at 1-, 2- and 3-years result 82%, 76% and 76%, respectively; BPFS 30%, 16% and 8%; PFS 13%, 5%, and 5%; OSRT 64%, 36% and 20% (Figure 1A). In various subgroups analysis, OSRT results significantly better when extracranial disease is controlled (Figure 1B).

Conclusion: In our experience, in line with literature data, stereotactic radiation therapy, regardless of primary, histology, location or fractionation, is an effective treatment for limited brain metastasis; survival from treatment mostly depends on extracranial disease status.

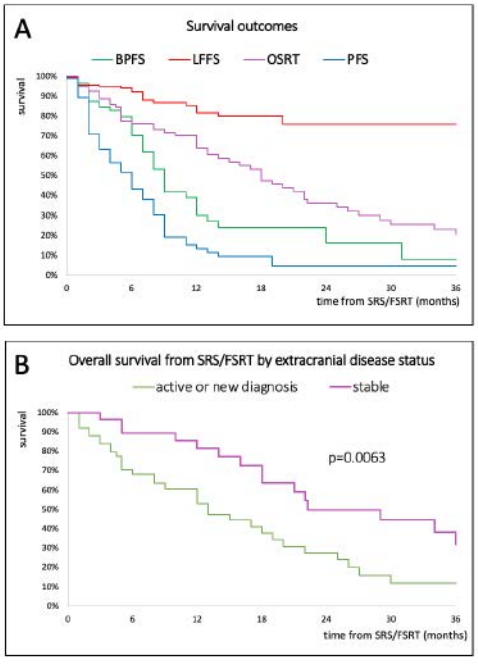

Figure 1. (A) Kaplan Meier curves of LFFS (red line); BPFS (blue line), due to both progression of BM treated or appearance of new lesions; PFS (green line) which may be due, in addition to brain progression, to extracranial one; OSRT (violet line). **(B)** Kaplan Meier curves of overall survival probability from RT between the two subgroups of patients with stable extracranial disease (violet line) and active or new diagnosis (green line). Log rank test showed a significantly ($p<0.05$) higher survival probability in the first group.

Figure 1.

P094

HYPOFRACTIONED RADIOTHERAPY FOR HIGH GRADE GLIOMAS WITH CONCOMITANT AND ADJUVANT TEMOZOLOMIDE: OUTCOME AND PROGNOSTIC FACTORS

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Aims: In this retrospective study we aimed to evaluate results and prognostic factors in patients with high grade gliomas treated with hypofractionated Radiotherapy (HYPO-RT).

Method: Patients with histologically confirmed high grade gliomas not fit for standard radiotherapy (RT), underwent to HYPO-RT + TMZ. Un-eligibility for standard RT were age (≥70 years), performance status (KPS<70), unresected or persistent disease after surgery. HYPO-RT was administered as 36Gy/12 fx or 40Gy/15 fx alone or concomitantly with TMZ. Adjuvant TMZ was administered in selected patients. Overall survival and Progression Free Survival were recorded and evaluated along with neutrophil/lymphocyte ratio (NRL), MGMT methylation, age, KPS, type of resection.

Results: From January 2013 to March 2022, 50 patients with high grade gliomas and median age of 66 years and median KPS of 80 were observed and treated at our institution. Among these 50 patients, 44 were Glioblastoma, 2 Anaplastic Astrocytoma and 4 had no histological diagnosis. Among operated patients, ten had complete resection, 34 partial, two a biopsy. MGMT methylation was recorded in 30 patients with 19 methylated MGMT promoter, and 11 without. Thirteen pts have an NRL ≤ 4, 36 pts > 4 and for 1 it was not possible to determine the blood count values. Thirteen pts received HYPO- RT only, 37 HYPO- RT+TMZ. One patient rapidly progressed during HYPO- RT with fatal event; 28 pts received adjuvant TMZ and 21 did not due to the rapid decline of the general conditions or disease progression. Median OS was 7.4 mo, while median PFS was 2.3 mo. Patients who had MGMT methylation had significantly longer overall survival than those without MGMT methylation [HR 0,24(95%CI 0,10-0,60)p 0,0022]; pts who had complete resection had significantly longer survival than those who had a partial resection [HR 0,37 (95%CI 0,14-0,95 p 0,0402]. In the NLR <4 group no statistical difference in OS *vs* the NLR>4 was found [HR 1,68 (95%CI 0,70-4,02)p 0,2377]. Also in the KPS ≥70 group no statistical differences in OS vs KPS <70 was recorded [HR 0,53 (95%CI 0,16-1,73)p 0,2994]. As regards PFS, patients who had MGMT methylation have a significantly better PFS than those without MGMT methylation [HR 0,33(95%CI 0,14-0,79)p 0,0128]. The other factors do not affected PFS. Twenty out of 50 pts (40%) received II line treatment (median PFS 3.16 mo): 14 pts underwent CHT alone (Fotoemustine and Bevacizumab or Regorafenib), 2 pts received Stereotactic radiotherapy (SRT) on progression site alone, while in 3 pts SRT and concurrent CHT was administered and 1 was candidate for surgery followed by CHT.

Conclusions: This cohort confirmed the results of HYPO-RT in older patients and in those with poor KPS or partially/unresected disease. An impact of resection and MGMT methylation was observed too. NLR did not have any impact on OS. Finally less than half patients received a second line therapy.

P095

INCIDENTAL DOSE TO LACRIMAL GLANDS IN PATIENTS TREATED WITH INTENSITY MODULATED RADIOTHERAPY FOR BRAIN TUMORS

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Aims: Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) leads to more painted dose distribution with increased ability to spare organs at risk (OARs) from high doses, but not from low doses. The impact of low doses is not negligible for small OARs, particularly in brain district where lacrimal glands (small organs deputed to moisten, lubricate and protect eye surface) may suffer from the actinic injury leading to dry eye syndrome and correlated ocular disorders. In this landscape, we analyzed the incidental dose to the lacrimal glands in patients submitted to brain radiotherapy (RT).

Methods: Twenty-one patients submitted to brain RT for high grade gliomas (HGG) and brain metastases (BM), between 2021-2022, were retrospectively evaluated. Prescribed dose range was 4005-6000 cGy (15-30 fractions) in HGG adjuvant RT, 24-27 Gy in 3 fractions in case of BM stereotactic radiotherapy. VMAT technique was applied in all treatment plan. Original plans did not include LG in the optimization process. Right and left LG were retrospectively delineated on MRI co-registered with planning CT (Figure 1) according to current guidelines. Constraints analyzed for each LG, according to available scientific literature, were; Dmax, Dmean, V15, V20 and V25. Biological equivalent dose to LG was calculated, in patients receiving an hypofractionated RT schedule.

Results: Median age was 50,4(24-79) years for HGG and 57,3 (42-79) for FSRT. Mean volume of LG was 0.825 cm3 (0-39-1.1). The average Dmax to the ipsilateral LG was 13.86 Gy (2–23.50 Gy) for HGG and 1,2 Gy (0,8-1,5 Gy) for FSRT; average Dmean was 598 cGy (118-798 cGy) for HGG and 70,1(81-154) cGy for FSRT. V15, V20 and V25 were respected in all plans; however

in 2 patients treated for HGG, a volume of 24-30% of LG resulted enclosed by isodose 15 Gy.

Conclusions: Although a variable association between radiation dose to the LG and incidence of dry eye syndrome is clear from scientific literature, the exact dose–response relationship remains unclear. V20 was identified as the most significant predictor of late toxicity while acute toxicity seems to increase with a Dmax >30.0 Gy. Because LG toxicity can negatively impact quality on life in surviving, could be interesting to investigate LG as emerging OAR. It plausible that treatment plan optimization for lens and optic nerve may contribute to preserve also LG. However, since the small sample size, further and prospective investigations are required

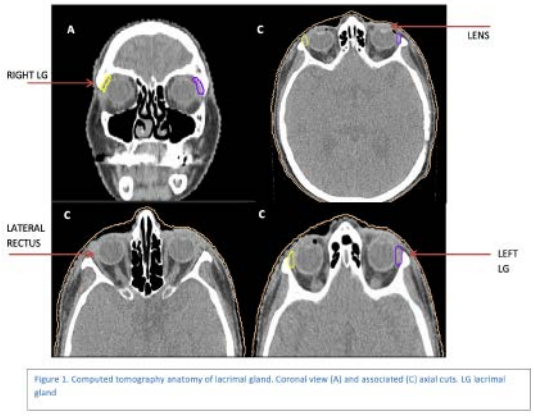

Figure 1.

P096

ROLE OF 18F-FET/PET TO OPTIMIZE RADIATION TARGET VOLUME IN HIGH GRADE GLIOMA

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Aim: In patients with a newly diagnosis of glioma, the 18F-FET/PET images may be useful to improve the radiotherapy target volume definition compared to standard MRI, in order to reduce toxicity and to avoid tumor missing. In this study were analyzed the differences between targets obtained from two different diagnostic methods (MRI and FET/PET) in patients who have to start the radio-chemotherapy treatment for high grade glioma.

Methods: From November 2021 to May 2022, 8 adult histologically confirmed high grade glioma were retrospectively analized. All patients underwent stereotactic biopsy or surgical resection and post-operative Radiotherapy treatment with Volumetric Modulated Arc Therapy (VMAT) technique associated with Temozolomide. Dose prescription was 60 Gy/30 fractions. OARs were delineated based on the RadiationTherapy Oncology Group (RTOG) contouring atlas. All patients had pre and postoperative MRI (T1-, T2- and FLAIR-weighted images) and postoperative 18-FET/PET. For all cases, after co-registration and fusion with simulation TC scan (slice3 mm), two RT treatment plans were created, one based on MRI data and the other one with 18FET/PET biological scans data. Subsequently the different volumes (PTVs) were compared volumetrically and spatially. The contouring and volume analysis was performed using FOCAL treatment planning software.

Results: Median age was 64 years (range 30-75), 5 patients was male (62%) and 3 female (38%), 3 have MGMT status + and 5 MGMT - Anatomical discrepancies were recorded between the PTVs of MRI and PET. PTV-18FET/PET was larger than PTV-MRI in 70% of cases, by a median volume of 52 ml (range 25-116) corresponding to a median increase in PTV volume of 4.69%. The spatial similarity volume was also low. In this experience PTV-18FET/PET has been shown to be useful to avoid geografical tumor misses in order to detected vital tumor more accurately.

Conclusions: This study showed that 18F-FET/PET exam combined with conventional neuroimaging may have an additional diagnostic value and may be useful in the therapeutic management of patients affected by glioma, suggesting a critically underestimation of the PTVs by contrast enhanced MRI. Future studies are needed for adoption of PET-guided delineation in radiotherapy treatment planning.

P097

CIRCULATING BLOOD CELL VALUE AS PREDICTOR FACTOR FOR OVERALL SURVIVOR IN BRAIN GLIOMA PATIENTS

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Aims: To investigate the role of neutrophil, lymphocyte, platelet and eosinophils as a prognostic factor for overall survival (OS) in patients with glioma grade II-IV according to WHO 2021.

Methods: We analyzed the clinical and hematological data of every consecutive patient treated from 2017 to 2021 with surgery and chemo-radiotherapy for high grade glioma (HGG), with a minimum follow up of 12 months. We collected neutrophil, lymphocyte, platelet and eosinophils value at 3 timepoints: diagnosis, after surgery and at relapse and related them with OS. Moreover, we try to evaluate if the changes of these values correlate with OS, according to MGMT methylation, IDH mutation and 1p19q codeletion.

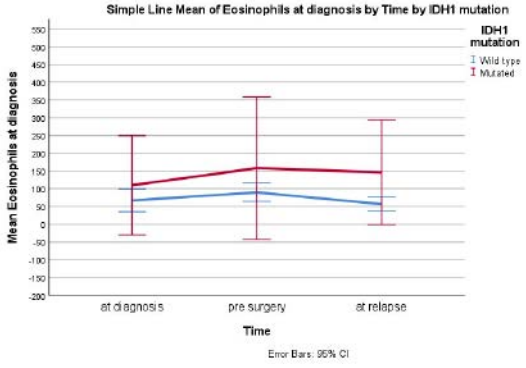

Figure 1.

Results: We evaluated a total of 62 pts (median age 61 years, range 27-81), 61.2% were men. The MGMT methylation status was found in 30 pts (48.4%), the IDH1 mutation in 13 pts (21%) and the 1p19q codeletion in 5 pts (8%). At diagnosis the neutrophil/lymphocyte ratio (NLR) did not correlate with OS (HR: 1.02, 0.96-1.10; p=0.62), also eosinophils/lymphocyte ratio and platelet/lymphocyte ratio were not predictors of OS (HR: 17.52 and 1.0, respectively). At a median OS of 15 months, the best cut-off for NLR was 3.47, with a sensitivity of 70.3% and specificity of 66.4% (AUC = 0.470); for eosinophils/lymphocyte ratio and platelet/lymphocyte ratio the AUC was respectively 0.176 and 0.451. In patients with IDH1 mutation that relapsed the absolute eosinophil values were statistically significant correlate with OS (P=0.001) (Figure 1). No correlation with MGMT methylation and 1p19q codeletion was detected.

Conclusions: From our analyses we did not find significant correlation between hematological parameters and OS. As regards pathological parameters further investigation on wider sample size are necessary to confirm our findings.

P098

ROLE OF CLINICAL FOLLOW-UP IN RADIOLOGICAL RESPONSE TO POSTOPERATIVE RADIOTHERAPY IN PATIENTS WITH HIGH-GRADE GLIOMA

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Aims: The aim of the study was to retrospectively analyze any differences between patients 'clinical conditions before and after radiotherapy (RT) especially the correlation with pseudo-progression and progression at MRI.

Method: We analyzed a retrospective cohort of patients with HGG (CNS WHO grade 3 and 4), treated from 2012 to 2021, at our Institute. All pts underwent surgery followed by RT with concomitant and/or sequential Temozolomide according to STUPP or hypo-fractionated protocol. We analyzed their clinical conditions at diagnosis, before RT, at first follow-up and at eventual relapse, focused on performance status (by ECOG scale), fatigue (CTCAE V5.0 2017) and neurological symptoms (scale 0 to 3, from asymptomatic to worsened, compared to diagnosis). At approximately 40 days after the end of RT, all pts underwent f.u. MRI to assess response to therapies according to RANO criteria (we considered stable disease in complete response (CR)), modified by addition of pseudo-progression. The same scale was used to identify disease progression.

Results: We evaluated a total of 52 pts (median age 61 years, range 27-78), 32 were men (61,5 %). At diagnosis 14 pts (26,9%) had single frontal lesion, 29 (55,7 %) left hemispheric lesions and 13 (25%) multicentric lesions. 29 pts (55,7%) had post-surgery residue. At diagnosis 33 pts (63,5%) had ECOG 0, 18 (34,6%) ECOG 1, 1 (1,9%) ECOG 3. After RT 23 pts (44%) had CR, 15 (28,8%) had pseudo-progression and 14 (26.9%) had real progression.

Four patients (7,7%) had pseudo-progression at following MRI control. 44 of 52 pts (85%) relapsed at a median time of 5 months (range 1-84), 43 pts (98%) relapsed in the tumour bed, 1 pts (2%) exclusively outfield. The median follow-up was 11 months (range 1-90). 35 pts (67.3%) died. Table 1 shows the monitoring of symptoms before the RT start, after the end of RT and at the time of relapse. Patients at pseudo-progression/CR show an improvement of neurological symptoms compared with diagnosis. Instead, relapse pts show an higher incidence of symptoms especially neurological one.

Conclusions: Our study, although limited by a retrospective design and small sample size, shows that especially neurological symptoms worsen at progression disease. At pseudo-progression symptoms improve or are stable as in patients with CR. This suggests the need for further in-depth clinical investigations to help us better characterize patients with relapse from those with pseudo-progression.

Table 1.

	Before RT	After RT	After RT	After RT	AT Relapse
	Overall	Complete response	Progression	Pseudo-progression	Overall
Number of patients	52	23 (44)	14 (28)	19 (36)	44 (85)
ECOG 0 (%)	29 (56)	18 (35)	4 (8)	13 (25)	16 (31)
ECOG 1 (%)	22 (42)	2 (4)	7 (13)	5 (9)	17 (33)
ECOG 2(%)	0	2 (4)	2 (4)	1 (2)	6 (11)
ECOG 3 (%)	1 (2)	1 (2)	3 (6)	0	5 (10)
ECOG 4-5 (%)	0	0	0	0	0
No neurological symptoms (%)	8 (15)	13 (25)	4 (8)	8 (15)	9 (17)
Stable neurological symptoms (%)	40 (77)	5 (9)	7 (13)	4 (8)	19 (37)
Improved neurological symptoms (%)	2 (4)	2 (4)	1 (2)	6 (11)	0
Worse neurological symptoms (%)	2 (4)	3 (6)	2 (4)	1 (2)	16 (31)
No fatigue (%)	42 (81)	15 (29)	11 (21)	14 (27)	29 (56)
Mild fatigue (%)	5 (9)	6 (11)	3 (6)	3 (6)	7 (13)
Moderate fatigue (%)	4 (8)	2 (4)	0	2 (4)	6 (11)
Heavy fatigue (%)	1 (2)	0	0	0	2 (4)

P099

HYPOFRACTIONATED RADIOTHERAPY (HYRT) IN ELDERLY (≥ 65 YRS) AND FRIAL GLIOBALSTOMA PATIENTS: OUR EXPERIENCE

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Aims: In GBM standard patients, surgery, radiotherapy (RT) plus concomitant and adjuvant temozolomide (TMZ) has resulted in longer survival as showed by Stupp'data. Elderly and frial pts affected by GBM generally are excluded by randomized studies, so the clinical guidelines are not so robust in defining the best treatment for these pts. We report our experience in terms of progression free survival (PFS) and overall survival (OS) in this setting of pts.

Methods: From 2019 to 2021 we treated 26 pts with HyRT of 40Gy in 15 fraction. Median age was 71 yrs and median postoperative KPS 80%. Sixteens pts underwent surgical resection, 10 received biopsy for diagnosis. Thirteen pts received concomitant TMZ, the other 50% were not eligible for TMZ because of frailty and comorbidities. All pts received HyRT with VMAT and two coplanar volumetric modulated arcs of 6MV energy with daily IGRT verification using CBCT and a robotic couch with 6 degrees of freedom. All pts were followed with Brain MRI and clinical evaluation each 3 mths. PFS was defined as time to progression or death from treatment and OS was defined as time to death from diagnosis.

Results: We divided our pts in 4 different groups basing on the received treatments. Group I (surgical resection + TMZ): 9 pts; Group II (only surgical resection): 7 pts; Group III (biopsy + TMZ) : 4 pts. Group IV (biopsy) 6 pts. In Group I, 3 pts are not still evaluable for follow-up, 2 pts had PFS> 11 mths, 2 pts had 6 mths PFS (one with a very good MRI partial remission), 2 showed rapidly progression disease. The median OS in this group was 11 mths. In Group II, 50% of pts showed a PFS>13 mths, but none reached a partial remission. The median OS in this group was 10 mths. In Group III, all pts showed a PFS≥8 mths with also one partial remission. The median OS in this group was 13 mths. In Group IV, the PFS mean was lower than all the other groups (3 mths) but, even among them, there was a case of MRI PR after 6 mths at last FU. The median OS in this group was 13 mths. Regarding toxicity, radiotherapy was well tolerated and no severe adverse events were reported.

Conclusions: GBM is a rapidly fatal illness, elderly and frial pts should be treated not only to meliorate OS and PFS, but also to preserve and respect their quality of life. HyRT seems to be an optimal and safety therapeutic choice. Surgery and chemotherapy are strongly influenced by comorbidities. Our data are in line with literature in terms of PFS and OS.

P100

NEWLY DIAGNOSED GLIOBLASTOMA: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: This study aims to evaluate the oncological outcome of patients treated for newly diagnosis of Glioblastoma (GBM) in terms of Overall Survival (OS), Progression-Free- Survival (PFS) and toxicity.

Method: From January 2017 to March 2022, clinical and imaging data of 176 patients with GBM treated at our Radiotherapy Department were analyzed. The majority of patients had undergone surgical resection followed by concurrent Temozolomide (TMZ) and radiotherapy (RT). Magnetic Resonance images (MRI) acquired before and after surgery, after radiotherapy and during follow-up were analyzed and used to define three categories of recurrence: in-field if >80% of the recurrent tumor was located within the 95% isodose surface; marginal if 20-80% of the recurrent lesion was within the 95% isodose surface; out-field if <20% of the recurrent lesion was within the 95% isodose surface. OS and PFS from the time of first diagnosis to recurrence were analyzed by the Kaplan-Meier method.

Results: 176 consecutive patients were evaluated: 113 male and 63 female. Median age at the time of first surgery was 63 (range 35 - 88). Mean Karnofsky Performance Status was 80. 7 patients underwent biopsy, 15 subtotal resection and 154 gross total resection (first surgery). Diagnosis of GBM was confirmed histologically in all patients. 135 patients were treated according to the Stupp protocol (RT 60Gy/30 ff and concomitant TMZ), while 41 patients received a hypofractionated RT schedule (40.05Gy/15F) plus concomitant TMZ. 71 of the 176 patients during follow-up presented a recurrence: 83% in field, 7% marginal and 10% out-field. 12 of the 71 patients underwent to second surgery followed by re-irradiation, 10 ones to re-irradiation alone, and 49 ones to chemotherapy. Re-irradiation doses ranged from 36 to 54 Gy in 18-27 fractions. No G2-G4 toxicities were observed. Median OS from first diagnosis was 82.5%, 55.8% and 40.6% at 12, 24 and 36 months respectively. PFS from primary treatment to re-irradiation was 57.7% and 39.2% at 12 and 24 months respectively. Median OS from re-irradiation was 50% at 7 months.

Conclusions: Our mono-institutional experience demonstrated that rates and patterns of recurrence of GBM after primary treatments and re-irradiation were similar to literature. Current knowledge confirms that GBM remains a poor prognosis disease; re-irradiation, alone or after second surgery, is safe and well tolerated.

P101

REIRRADIATION IN RECURRENT MENINGIOMAS

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Aims: Probability of recurrence of meningiomas varies depending on WHO grade (up to 84% in grade III at 5 years). For recurrent disease, standardized guidelines still lack and treatment is guided by local experience and clinical practice. We performed a retrospective analysis of data about survival and safety in a cohort of patients with recurrent meningioma who underwent reirradiation.

Tables 1-2-3.

Table 1

Age at reirradiation (range)	66 (59-77)
KPS at reirradiation (range)	88,4 (70-100)
Localization:	
- Convexity	68,4% (n=13)
- Falcine/parasagittal	15,7% (n=2)
- Anterior fossa skull base	10,5% (n=3)
- Middle fossa skull base	0% (n=0)
- Posterior fossa skull base	5% (n=1)
WHO grade	
- I	0% (n=0)
- II	36,8% (n=7)
- III	5% (n=1)
- no histological confirmation	57,9% (n=10)
Prior treatment	
- Surgery	95% (n=18)
- Radiotherapy	5% (n=1)
Surgery at progression	
- Yes	7% (n=7)
- No	11% (n=11)

Table 2

Technique	1^ RT	2^ RT
EBRT	63%	10%
IMRT	0%	10%
multi-fraction SRS	5%	10%
single fraction SRS	32%	70%

Table 3

	1^ course RT mean (range)	2^ course RT mean (range)
GTV cc (range)	19,6 (6-55,5)	12,34 (0,41-33,94)
Tumor EQD2	54,9 (27,5–142,5)	32,34 (16-557,42)
Tumor BED (range)	82,3 (41,2-213,7)	131,4 (96,5-261,75)
Brain EQD2 (range)	58,8 (56-61,5)	55,4 (44,9-64)
Brain BED (range)	71,79 (20,5-123,1)	229,9

Methods: Between 1995 and 2021 we collected data of 19 continuous recurrent meningioma patients who underwent reirradiation at our center. As first treatment,

18 (95%) patients underwent surgery. First radiotherapy (RT) was delivered as adjuvant therapy, at recurrence and as prior treatment in 7, 11 and 1 cases, respectively. At recurrence, 36,8% of patients underwent a second surgery. Other patients' characteristics can be found in Table 1. We estimated the biologically equivalent doses in 2 Gy fractions (EQD2) for normal tissue and tumor (a/b =2 for brain tissue and a/b = 4 for tumor). Radiotherapy techniques and dosimetry are listed in Table 2 and 3 respectively. The primary outcome was progression-free survival (PFS); secondary outcomes included overall survival (OS) and treatment-related toxicity. Toxicity was assessed according to Common Terminology Criteria for Adverse Events version 5.0. Kaplan–Meier curves were generated to examine the effect of several parameters on PFS; Logrank test comparison was used to determine predictors of PFS.

Results: With a median follow-up of 117.7 months, the median PFS and OS observed were 22.8 and 119.1 months, respectively. We found that PFS was longer if BED was lower (23.99 and 18.33 months if BED under or over 131.4, respectively, p 0,81). PFS was longer in patients that didn't undergo a second surgery (25.2 vs 19.0 months, p 0,27). Finally, the presence of alterations at magnetic resonance performed after RT, demonstrated rates of shorter PFS (13.6 *vs* 24.4 months, p 0,2). After reirradiation, we observed 2 cases of G1 acute toxicity (any kind of toxicity), 1 for G2 and 1 for G3. In chronic, we only registered 1 case of G1 toxicity and 2 cases of G2.

Conclusions: Reirradiation in recurrent meningiomas shows promising results in terms of safety and toxicity profile. Maybe due to the small number of cases, we didn't find any statistically significant correlation between dosimetric parameters and PFS; prospective studies and larger populations are necessary to assess definitive efficacy of this treatment.

P102

STEREOTACTIC RT FOR RECURRENT GLIOBASTOMA: INITIAL EXPERIENCE IN SINGLE CENTER

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Aims: Glioblastoma (GBM) is primary central nervous system tumor associated with poor prognosis, even after primary trimodal treatment with a very high tumor recurrence rate. We report our initial experience with some dosimetric considerations.

Methods: From 2019 to 2022, we re-irradiated 8 recurrent GBM pts, according to RANO (response assessment for neuro-oncology) criteria. Six male and 2 female, median age at the first diagnosis 54 yrs (range 38-62). At the time of recurrence, pts were evaluated for salvage treatment based on clinical conditions, tumor site and volume, time to recurrence, by a multidisciplinary team. All pts were previously and homogeneously submitted to the STUPP protocol. All pts were treated with two coplanar VMAT arcs and 6MV with daily IGRT verification using CBTC and a robotic couch with 6 degrees of freedom. All pts were followed with Brain MRI and clinical evaluation each 3 mths The median time to progression was 19 mths. All pts showed a recurrence in field during the follow-up. For retreatment, computed tomography simulation was executed with a 1.25-2.5 mm slice thickness. A co-registration of volumetric CT plus MR sequences (enhanced T1, Flair and T2) plus PET DOPA was used to define the target (GTV) and organs at risk (OAR). PTV was obtained with 2÷3 mm margin expansion. The median volume of GTV was 11 cc and the median volume of PTV was 44,65 cc. Four pts were treated with concurrent TMZ, 4 without. The retreatment prescription dose was 30Gy in 6 fx prescribed to the isodose line of 80%. Treatment was performed using 5 non coplanar arcs to change the beam's entry and to spare OARs, to respect normal brain, optic apparatus and brainstem dose constraints. We used flatness filter free energy of 6MV. For all the pts, we performed EQD2 plans to evaluate OAR's summed dose.

Results: Dose to normal brain tissue represents the most important limiting aspect because of the risk of necrosis following the reirradiation. As reported in literature this risk arises when cumulative EQD2 for normal tissue brain exceeds 137Gy. The median EQD2 dose to normal brain tissue was 106Gy (range 81-132 Gy). The median doses to optic apparatus and brainstem were 16Gy (range 4–43Gy) and 35Gy (range 7–49 Gy). All treatment plan showed a good target coverage (isodose 80% up to 98% PTV).

Conclusions: Our preliminary data showed the respect of OARs constraints and PTV coverage. We'll analyze the brain toxicity due to reirradiation.

P103

CRANIAL REIRRADIATION IN PRIMARY BRAIN TUMORS: A SINGLE CENTER EXPERIENCE

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Aims: Cranial re-irradiation(CR) and its complications is an important topic for the increase in survival and the improvement of radiotherapy techniques. However, the safety and efficacy of CR are debated topics. We aimed to assess toxicity and adverse events (AEs) in a

cohort of patients affected by primary brain tumors who received CR and analyzed dosimetric and clinical data of patients receiving CR, using doses and volumes.

Method: We retrospectively analyzed the data of 26 patients who received CR from 01/2007 to 05/2021(53.8% glioblastoma, 15.5% astrocytoma, 3.8% gliosarcoma, 3.8% anaplastic glioma, 23.1% oligodendroglioma). RT-related AEs were retrospectively evaluated and analyzed according to cranial RT type and timing of RT and radionecrosis was evaluated by magnetic resonance imaging.

Results: In total 26 patients had at least 2 courses of intracranial radiotherapy. All patients received standard treatment at first course concomitantly with Temozolomide. The mean dose was 60 Gy. During second course all patients underwent hypofractionation (3 patient -11.6%- 39.9Gy/2.66 Gy per fraction, 3 patient -11.6%- 20Gy/5 Gy per fraction, 14 patient -53.8%- 25Gy/5 Gy per fraction, 5 patient -19.2%- 30Gy/6 Gy per fraction, 1 patient -3.8%- 35Gy/5 Gy per fraction). The mean volume irradiated at the first course was 234,84 cc and at the second course was 81,7 cc. No patients experienced acute-AE although 96.1% were on antiepileptic therapy. Three patients reported severe asthenia and one patient (3.8%) reported a single episode of dizziness during treatment. We observed 3 radionecrosis (11.5%) after a median time of 11.7 months, however asymptomatic. Median survival is 27.1 months from the diagnosis.

Conclusions: Repeated radiotherapy appears safe in patients with recurrent primary. The goal is to frame the radionecrosis also in the light of the new evidence in the comparison of MRI and with amino acid PET. However, further studies are needed in order to establish the correct dose prescription in relation to volume.

P104

DIFFUSE MIDLINE GLIOMAS: EXPERIENCE OF SINGLE CENTER

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Aims: Diffuse midline glioma with H3K27M mutation is a new tumor type of WHO central nervous system tumor classification. It is a rare subtype of glial tumors in adult. We report three cases of diffuse midline glioma in young adult.

Methods: From March 2020 to June 2021, we treated three young adult, respectively two female (patient A 26 yrs-old and patient B 36 yrs-old) and one male (patient C 24 yrs-old), affected by diffuse midline glioma. All patients underwent a partial resection. Pathological examination results were: 2 G2 and 1 G3 astrocytoma, respectively. In all cases, molecular and histological revisions showed GBM IDH wildtype, H3K27M positive. After surgery, the patients received different radiotherapy scheme and concomitant and adjuvant temozolomide. Patient A received a total dose radiotherapy of 39.9 Gy in 15 fx. Patient B and C a total dose of 56 Gy in 28 fx. Patient C had a diagnosis of PNET IV when he was 12 yrs old. He underwent surgery plus chemotherapy plus radiotherapy. After 3 yrs the FUP with MRI Brain examination, a new diffuse midline glioma was diagnosed. We treated all the tree patients with VMAT, with two coplanar volumetric modulated arcs and 6mMV energy, with daily IGRT verification using CBCT and a robotic couch with 6 degrees of freedom.The different dose prescriptions (39.9 Gy/15 fr or 56 Gy/28 fr) were based on the target volumes and positions to respect OAR dose costraints.

Results: Patient A had a progression disease after 1 yr and she started systemic II line therapy with Regorafenib. After 27 mths, she has stable disease. After initial radiological response, patient B had a progression disease with leptomeningeal dissemination after 1 yr, therefore she is, now, receiving best supportive care. Patient C had a good response with partial remission up to now.

Conclusions: We report three cases of adult diffuse midline glioma with H3K27M+ with different response to the therapy.

P105

REDUCTION OF PAROTID GLANDS DOSE IN HIPPOCAMPAL SPARING WHOLE BRAIN RADIOTHERAPY WITH HELICAL TOMOTHERAPY

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Aims: An estimated 20% of patients with cancer will develop brain metastases. the prognosis of these patients is improving with new therapies so it is important to improve their quality of life. Hippocampal avoidance during whole brain radiotherapy has been investigated by the RTOG0933 and memory and neurocognitive function preservation was reported. A reduction of parotid gland dose is also necessary to prevent xerostomia. The aim of our analysis was to evaluate the dosimetric impact of Helical Tomotherapy (HT) in reducing parotid gland and hippocampal doses in whole brain radiotherapy.

Method: Five patients with brain metastases who previously underwent 3D whole brain radiotherapy were

enrolled. The whole brain was delineated as the clinical target volume (CTV) and a planning target volume (PTV) was created by adding an isotropic 5 mm margin. The hippocampus was delineated with CT/MRI image fusion. HT planning with the Raystation® 10A version was performed on PTV-f, defined as the difference between PTV and hippocampal expanded by 5 mm. All patients were treated with a dose of 30Gy in 10 fractions. Dose optimization for HT treatment plans was applied to respect RTOG0933 constraints: for PTV-f D2% <37.5Gy, D98% >25Gy, for hippocampus D100% <9Gy, Dmax < 17Gy. Furthermore a Dmax < 5Gy was considered for the lens and a Dmean < 25Gy was considered for the parotid glands. For both plans (3D-CRT and HT) the mean doses for hippocampus and parotid glands, the maximum doses for lens were extracted and compared using the Wilcoxon-Test.

Results: PTV coverage was reached for both 3D-CRT and HT treatment plans with a D98 always >25 Gy. All HT treatment plans fulfill RTOG0933 hippocampal constraints of at least one hippocampus. Doses to parotid gland and hippocampus are shown in Table1. The mean dose to bilateral parotid glands was reduced from 7.0 Gy to 5.0 Gy using 3D-CRT and HT respectively ($p<0.001$). The mean dose to hippocampus was reduced from an average of 29.4 Gy with 3D-CRT to 14.8 Gy with HT ($p<0.001$). Lens Dmax was reduced from an average of 3.2Gy with 3D-CRT to 2.7Gy with HT (left) and from an average of 3.3Gy with 3D-CRT to 2.7Gy with HT (right) ($p<0.001$).

Conclusions: Our dosimetric analysis showed a great advantage of helical tomotherapy in hippocampus sparing whole brain radiotherapy with minimal doses to hippocampi and to parotid glands. HT should be considered as a valid approach to reduce cognitive decline and xerostomia improving quality of life for selected patients who require whole brain radiotherapy.

Mean Dose Parotid_L (cGY)		Mean Dose Parotid_R (cGY)		Mean Dose Hyppoc_R (cGY)		Mean Dose Hyppoc_L (cGY)	
3D	TOMO	3D	TOMO	3D	TOMO	3D	TOMO
1007	889	1191	855	2936	1373	2926	1364
817	497	599	290	2980	1405	2977	1409
221	193	241	183	2909	1510	2929	1530
1373	803	720	572	2966	1663	2971	1650
451	346	389	349	2927	1506	2921	1409

Figure 1.

P106

RADIO-CHEMOTHERAPY RE-TREATMENT IN PATIENT WITH HIGH GRADE GLIOMA

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Method: In March 2010, the patient underwent emergency head CT(computed axial tomography) after trauma accidental skull without loss of consciousness, showing the presence of lesion new formation at the level of the right semi-oval center with marked periwound edema and mass effect on the furrows .The subsequent nuclear magnetic resonance (MRI) confirmed the presence of such lesion. The patient was then subjected to a stereotaxic biopsy of the lesion he posed diagnosis of III degree anaplastic astrocytoma. In May 2010 the patient underwent exeresis of the known formation (histological confirmation of astrocytoma anaplastic grade III) with subsequent radiotherapy (6000 cGy in fractions of 200 cGy at the level of surgical bed +2 cm of expansion) concomitant with temozolomide 75 mg/m^2 daily The patient was also subjected to 12 cycles of temozolomide 200 mg/m^2 G1-5 q28. Following exclusive follow up mIn July 2020, evidence of disease progression posterior to the surgical cavity. On September 2020 MRI further parietal progression with a small deep pericallosal nodule. It is was subjected again on 05/10/2020 to exeresis of the lesion (Glial neoplasia diffuse with area consistent with focal anaplastic astrocytoma, grade III associated with post-actinic changes and high-grade diffuse glial neoplasm consistent with IDH-mutated glioblastoma, grade IV methylated MGMT, mutated IDH1). Post-operative disorder praxis to left hemisome improved after motor rehabilitation. New postoperative adjuvant treatment with radiotherapy (4400 cGy in fractions of 200 cGy a surgical bed level + 2 cm expansion) concomitant with temozolomide 75 mg/m^2 daily with subsequent 6 cycles of temozolomide 200 mg/m^2 G1-5 q28.

Results: As of June 2022 the patient is disease free with moderate left limb paresis with spastic hypertonus especially lower.

Conclusions: Reirradiation concurrent with temozolomide can be a particularly effective weapon in management relapses of high-grade glioma recurrence.

P107

RADIOLOGICAL MEASUREMENTS TO PREDICT DOSE VARIATION DUE TO INTER-FRACTION VARIABILITY IN HEAD AND NECK TREATMENTS

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Aims: As a new discipline, online Adaptive RadioTherapy (ART) requires new indicators to quantify the impact of inter-fraction variations on dose distribution, thus allowing identification of the optimal time to

switch towards (online or offline) ART approaches. In this experience, a predictive model was proposed to early identify treatment fractions where unacceptable dose variations may be present in patients (pts) affected by head and neck squamous cell carcinoma (HNSCC).

Method: A total of 14 pts were treated using an Artificial Intelligence (AI)-based linac, acquiring a daily positioning CBCT image without online adaptation, prescribing 70 Gy in 35 fractions or 60 Gy in 30 fractions. For each patient, all CBCT images acquired for patient positioning were rigidly matched to the planning CT (pCT). Daily CBCT images were automatically recontoured and treatment plans were recalculated on the corresponding synthetic CT. The variation of V95% of PTV_HR and max dose of spinal cord from the original values reported on pCT were collected along with the treatment: fractions where PTV V95% decreased by 3% and spinal cord Dmax increase of 3% were considered as needed of ART. The following radiological parameters were measured on each daily CBCT aligned with pCT to quantify the inter-fraction variability present in each RT fraction once compensated for couch shifts: the absolute body variation along AP and LL directions was measured in the proximity of the plans passing through different vertebrae (C2, C3) and the corresponding discs (C2-C3, C3-C4). The correlation between such parameters and the fractions needed for adaptation was investigated using the Wilcoxon Mann Whitney test and a logistic regression model was created.

Table 1.

BODY VARIATION IN LL DIRECTION AT C2-C3 DISC (MM)	PROBABILITY OF FRACTION REQUIRING ADAPTATION
1	59,1%
2	66,8%
3	73,8%
4	79,7%
5	84,5%
6	88,4%
7	91,4%
8	93,7%
9	95,4%
10	96,6%

Results: On the basis of the predefined criteria, the 212/400 fractions analysed required online adaptation. At the univariate analysis,, the most significant parameter was the body variation along the LL direction measured through the C2 disc (p=0.0017). Table 1 reports the probability of obtaining a fraction requiring online adaptation on the basis of the body variation in LL direction, obtained thanks to the predictive model developed.

Conclusions: A new metric to define the need for ART was proposed based on body variation measured along the LL direction through the C2-C3 disc: if such value results > 5 mm the treatment fraction has to be considered needed of ART (85% of probability of not meeting the tolerance criteria).

P108

IMPACT OF RADIOTHERAPY ON THE INCIDENCE OF IMMUNE-RELATED HYPOTHYROIDISM IN PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Aim: The purpose is to assess the impact of previous radiotherapy (RT) on the incidence of Immunotherapy(IT)-related hypothyroidism in patients (pts) with head and neck squamous cancer (HNSCC).

Methods: This is a retrospective single-center cohort of HNC pts who received IT treatments in recurrent and metastatic settings of disease. Tumors of the oropharynx, larynx, hypopharynx, oral cavity, paranasal sinuses and squamous cell carcinoma metastatic to the cervical nodes with an unknown primary (CUP) were included. Administration of radical and adjuvant RT with a total fractionated dose >50 Gy was allowed. As for IT, we included pts who received nivolumab, pembrolizumab and atezolizumab (alone or in combination with chemotherapy). Pts underwent at least 3 cycles of IT and a periodic evaluation (3 months) of thyroid function plasmatic tests. Hypothyroidism was scored according to CTCAE v5.0. A chi-square test of independence was performed to examine the relation between RT and the incidence of grade (G) 1-2 hypothyroidism.

Results: Seventy pts treated with IT from 2018 to 2021 were analyzed. Overall, 15 pts received less than 3 cycles of IT and were excluded from the final analysis. Twenty-nine pts underwent prior RT (RT-IT group) and 26 received IT alone (IT group) (Table 1). Sixteen pts developed G1-2 hypothyroidism (29.1 %). Eleven pts in the RT-IT group and 5 pts in the IT group developed G1-2 hypothyroidism (37.9% and 19.2%, respectively). The incidence of hypothyroidism in the RT group was higher in pts undergoing RT for larynx (66.6%), CUP (66.6%), oropharynx (50%) and hypopharynx (50%) primaries whereas pts receiving RT for cancers of the oral cavity and paranasal sinuses had fewer events (11.1% and 0%, respectively). We reported no significant difference in the incidence of hypothyroidism between RT-IT and IT groups when taken as a whole (p=.13). A higher risk of immunotherapy-related hypo (p=.012) was observed in those patients who were irradiated for HNSCC primaries where the thyroid gland could not be spared from medium-high doses. Further dosimetric analyses are ongoing to define a dose-volume threshold of clinical relevance.

Conclusions: The receipt of full course RT was corre-

lated with a higher incidence of hypo during IT, suggesting the need of closer monitoring of thyroid function in these pts. More studies focusing on dosimetric assessment are needed to confirm the correlation between prior RT and the onset of IT-related hypothyroidism.

Table 1.

Characteristic		RT-IT group	IT group
Number of patients		29	26
Age	<60	13	1
	60-70	8	5
	70-80	6	9
	>80	2	11
HNC localization	Oropharynx	10	4
	Larynx	3	1
	Hypopharynx	2	2
	Oral cavity	9	14
	Paranasal Sinuses	2	5
	CUP	3	0
Type of IT	Nivolumab	19	13
	Pembrolizumab	8	13
	Atezolizumab	2	0
Hypothyroidism	Yes	11	5
	No	18	21

P109

INFLUENCE OF RADIATION DOSE ON PATIENT-REPORTED ACUTE TASTE IMPAIRMENT IN A PROSPECTIVE OBSERVATIONAL STUDY COHORT IN HEAD AND NECK SQUAMOUS CELL CANCER (HNSCC)

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Aims A common acute side effect of radiotherapy in HNSCC patients is taste alteration (TA). Aim of our work was to evaluate dosimetric parameters related to patient-reported TA and quality of life in a prospective cohort treated with intensity-modulated radiotherapy (IMRT).

Methods: Eligible patients had locally advanced HNSCC suitable to curative treatment. Scores for TA were extracted from Chemotherapy-induced Taste Alteration Scale (CiTAS), EORTC QLQ-C30 and QLQ-HN43 questionnaires at baseline (T0), 3 weeks after radiotherapy conclusion (T1) and 3 months after treatment (T2). Base of tongue (BOT), submandibular glands (SG), parotid glands (PG) and taste buds were delineated according to consensus guidelines; a prospective consensus delineation of three independent physicians was obtained with internal consistency by dividing the remaining tongue into an anterior and middle third. The mean dose to the above-mentioned volumes was correlated with patient-reported outcome.

Results: Between September 2019 and November 2020, 33 patients were recruited, 31 of which analyzed. 71% had oropharyngeal tumors, mostly HPV-related (60%). All were treated with Tomotherapy. 77.4% had concurrent cisplatin. The mean scores of CiTAS subdomains, global health status and dry mouth and sticky saliva at T0, T1 and T2 are reported in Table 1. The mean doses to the anterior third, middle third and base of the tongue were 23.85 Gy, 35.50 Gy and 47.67 Gy, respectively. Mean dose to the taste buds was 32.72 Gy. Right and left parotid received 25 Gy and 23 Gy; right and left submandibular glands 47.8 Gy and 39.4 Gy. At univariate analysis, TA was related with SG mean dose (95% CI 0-0.02 p=0.05) and PG mean dose (95% CI 0-0.02 p= 0.05); dry mouth with mean dose to anterior (95% CI 0.03-1.47 p=0.04) and medium third (95% CI 0.02-0.93 p=0.04) of the tongue, to taste buds (95% CI 0.06-0.96 p=0.03) and to SGs (95% CI 0.06-0.63 p=0.02); pain mouth correlated with mean dose to taste buds (95% CI 0-0.02 p=0.04) and to base tongue (95% CI 0-0.02 p=0.02).

Conclusions: Our hypothesis-generating study supports impact of dose distribution to HN region to TA. The influence of dose to taste buds and tongue subvolumes remains unclear and warrants further investigation.

Table 1. Mean scores of CiTAS subdomains, dry mouth and sticky saliva and QoL at T0, T1 and T2.

	T0	T1	T2
Taste alteration (CiTAS)	1.17	2.59	1.83
Phantogeusia and Parageusia (CiTAS)	1.14	2.65	1.78
Taste discomfort (CiTAS)	1.28	2.01	1.53
Taste reduction (CiTAS)	1.30	3.01	2.19
Dry mouth and Sticky saliva (H&N43)	11.29	49.46	46.67
Global Health Status (C30)	69.35	62.37	71.39

P110

SALIVARY GLAND TUMOURS: RESULTS OF THE TRENTO PROTON THERAPY CENTRE

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Aims: Salivary Gland cancer (SGC) is a rare and heterogenous group of tumors. The treatment of salivary gland tumors is challenging, as randomized trials for this entity are rare. Radiotherapy is often applied after surgery for locally advanced tumors; in particular cases it can be used in a radical setting. We report the experience in treating salivary gland tumors with proton therapy (PT)

Method: Between June 2015 and June 2022, 69 patients (pts) have been treated with PT. Median age at PT was 55 years (range, 23-90). Median KPS was 90 (80-100). The most represented stage were stage III and IV. Parotid gland was involved in 47 cases, submandibular in 12, minor sites in 10. 32 patients presented perineural invasion. Pathology was: 37 adenoid cystic carcinoma, 12 mucoepidermoid carcinoma, 3 SCC, 2 adenocarcinoma ex pleomorphic adenoma, 5 pleomorphic adenoma, 10 others. Twenty pts received more than one surgical resection, 2 pts had biopsy only, the remaining ones received only one surgery. 55 pts were treated in adjuvant setting (17 R0; 34 R1; 4 R2), 4 with definitive intent, 10 were reirradiation. Acute and late toxicities have been reported according to CTCAE scale version 5.0.

Results: Median follow-up was 16 months, all pts but one completed their treatment without any break due to acute toxicity. PT was delivered in all cases with single field optimization-active scanning technique. Median total dose was 65 Gy(RBE) (range, 45-70.4 Gy(RBE). PT Re-RT median dose was 66 Gy(RBE) (range 60-70 Gy(RBE). No acute toxicity > grade 3 was observed. Grade 3 acute cutaneous toxicity was seen in 26 pts. Oral and sinonasal mucositis of grade 3 occurred in 3 pts. Cutaneous G1 late toxicity was seen in 19 pts, no cutaneous late toxicity > grade 2 was observed. 5 pts developed edema,18 pts fibrosis of the subcutaneous tissues and 7 pts cutaneous telangiectasia G1. Four cases of trismus G1 were reported. One pt developed oro-nasal fistula. At the time of the analysis, 48 pts are free of disease, 8 pts have stable disease, 7 pts in local control developed distant metastasis, one pt show a local and distant progression and one pt only local progression. Two pts died for distant metastasis.

Conclusions: Treat salivary gland tumors with PT showed to be feasible and safe; outcomes are encouraging. Longer follow-up is required to better evaluate the durability of local control and the possible development of late toxicities.

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DOSIMETRIC COMPARISON OF ORGANS AT RISK USING TWO DELINEATION GUIDELINES FOR THE RADIATION TREATMENT OF CT1 LARYNGEAL CANCER

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Purpose: A number of contouring methods have been used for the delineation of the primary tumor clinical target volume (CTV-P) in Head and Neck Cancers. They include the "anatomic method" proposed by Lapeyre and colleagues the so called French contouring *Methods:* More recently an international guidelines proposed by Gregoire and colleagues tried to integrate the anatomical method with the "geometric methods" proposed by the DAHANCA group in a single contouring method. This new contouring guideline may have the interesting characteristic to obtain reduced contouring volumes with respect to the French method with the potential to spare the surrounding organs at risk (OARs) especially in cT1 GC. This specific aspect is important since factor influencing the choice between radiotherapy and for the treatment of glottic cancer (GC) is focused not just on oncological outcome but also on reduction of treatment related toxicity. Our objective is to compare the OARs sparing properties of plans generated by VMAT of the French and the International consensus contouring methods in laryngeal SCC.

Methods: Ten CT of patients with T1 GC were contoured using the two contouring guidelines. For all cases, the GTV was delineated by a single radiation oncologist. The OARs were outlined and VMAT plans were generated. Dosimetric parameters of OARs, carotid arteries (CAs) and carotid bulbs (CBs) were compared.

Results: The target volumes contoured by the two delineation methods were VMAT plans translated into dose distributions favoring the International guidelines. Better dosimetric sparing was observed for spinal, supraglottic larynx, cricopharyngeal inlet, thyroid gland and medium and inferior PCM. Mean ipsilateral CBs and CAs D0,1cc were lower in VMAT plans generated from the International guidelines. Similarly, contralateral CBs and CAs D0,1cc, Dmean and V35 were spared after the use of the International guidelines.

Conclusions: The use of the International guidelines of Gregoire and colleagues translated into dosimetric advantages in OARs sparing showing large differences in CTV delineation between the 2 delineation nethods.

P112

EVALUATION OF RADIOTHERAPY DOSES TO CONSTRICTOR MUSCLES IN HEAD AND NECK CANCER PATIENTS AT HIGH RISK OF DEVELOPING DYSPHAGIA AFTER MULTIMODAL TREATMENT

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Aims: In the last decade, the outcomes of patients affected by head and neck cancer have increased thanks to the optimization of multimodal therapeutic strategies. The side effects related to the treatments can affect the quality of life of patients with the development of sequelae such as dysphagia, even in very young patients. Highly conformational techniques have partially reduced side effects, but they remain significant due to the large treatment fields. After recontouring these structures, we evaluated the relationship between the planned dose and the constrictor muscles of the pharynx and the cricopharyngeal muscle.

Methods: In our department between February 2017 and March 2019, 84 patients with histological diagnoses of head and neck tumors were treated with IMRT or V-MAT . A pre-treatment complete history and clinical evaluation were collected for each patient. Forty-five patients were considered at high risk to develop dysphagia due to indications of use high radiation doses and bilateral neck irradiation. We analyzed this group of patients, whose characteristics are shown in the table. The constrictors of the pharynx and the cricopharyngeal muscle were recontouring according to guidelines. Toxicity was assessed weekly during radiotherapy, one month after treatment, and every three months after that. The correlation between acute (<6 months) and chronic (> 6 months) toxicities was then related to dosimetric values. The t-test was used to correlate the onset of dysphagia with the calculated dose.

Results: No acute or chronic grades of toxicity ≥ 4 have been reported. Despite the acute onset of G3-dysphagia was in 15 (30%), it persisted in only five patients (6%) at one year. The rest of the patients (70%) reported acute onset of grade < 2 toxicity, while the percentage of chronic dysphagia of any grade dropped to 20%. The onset of acute grade 3 dysphagia correlates with mean doses > 50 Gy to any muscles, while the persistence of grade 3 dysphagia after six months correlates with a mean dose > 55 Gy to inferior constrictor and cricopharyngeal muscle.

Conclusions: The superior constrictor seems to have a minor role in the onset of late dysphagia. The limited number of patients and the lack of evaluation of the other structures related to the swallowing process do not allow definitive results on the importance of respecting the constraints of the more caudal pharyngeal muscles concerning the persistence of dysphagia.

Table 1.

Patient Characteristics n=45	Median (Range)
Age	67 (41-84)
Primary site	Oropharynx 16(35.4%) Oral cavity 6 (13,3)% Larynx 15 (30%) Nasopahrynx 6 (13,3%) Unknow primary 4 (8%)
T stage T1+T2 T3+ T4	18 (40%) 27 (60%)
N stage N0 N1+	12 (26,6%) 33 (73,4%)
Radiotherapy Radical Adiuvant	30 (70%) 15 (30%)
Chemiotherapy	No 9 (20%) Concurrent 33 (73.3%) Induction+concurrent 3 (6.7%)

P113

STEREOTACTIC BODY RADIOTHERAPY IN ELDERLY PATIENTS WITH INOPERABLE PRIMARY HEAD AND NECK CANCER: A SINGLE CENTER CLINICAL EXPERIENCE

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Aims: In elderly patients, it is strictly necessary to identify odynophagia and dysphagia to avoid malnutrition, dehydration, and cachexia, especially in head and neck cancer. There was evidence that conventional local treatments, such as surgery and/or external beam radiotherapy ± chemotherapy, can significantly impact also the quality of life. Hypofractionated stereotactic radiotherapy (SRT) could be an alternative strategy for frail head and neck cancer.

Methods: From 2019 to 2021, our department treated twelve elderly patients with locally advanced head and neck cancer with SRT. Morphological and functional imaging was employed to define the treatment volume. Patients were discussed on a case-by-case basis by the Multidisciplinary Committee on Head and Neck Cancer. All were unsuitable for surgery and/or standard radiotherapy +/- chemotherapy due to frailty. SRT consisted of 40

Gy in five daily fractions. All patients were initially evaluated with the NRS scale for odynophagia and dysphagia at the start of treatment and 1-month follow-up visit after SBRT, and subsequently for routine follow-up visits every three months.

Results: The mean age was 84 (range 78-96 years), seven males and five females. The primary sites were oral cavity in 5 patients, oropharynx in 4 patients and parotid glands in 3 patients. 50% were AJCC stage III, 30% stage IVA, and 20% stage IVB. The mean follow-up was ten months (range 1-24 months). Odynophagia was assessed with the numerical rating scale (NRS). We collected NRS before therapy, at 1-month follow-up, and at last FUP visits. Before treatment, all patients had severe pain between 7 and 8 NRS scale. At one month, there were three patients (25%) with an NRS 8, one patient (8%) with NRS 5, three patients (25%) with an NRS 4, and the remaining five patients had an NRS 3. This pain control allows us to reduce the medication dose in all patients, but 2. Fifty percent had an objective response, and 30% had stable disease, with overall survival of 10 months. No patients showed significant toxicity.

Conclusions: In our experience, elderly unresectable HNSCC patients treated with a short-course RT can obtain effective pain control and avoid a medication overload.

P114

FEASIBILITY OF ADJUVANT EXTERNAL BEAM RADIOTHERAPY AFTER METABOLIC RADIOTHERAPY WITH 131-I IN LOCALLY ADVANCED DIFFERENTIATED THYROID CANCER: AN INTERDISCIPLINARY MONO-INSTITUTIONAL EXPERIENCE

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Purpose/Objective: Adjuvant external beam radiotherapy, after radiometabolic therapy with 131-I, for differentiated thyroid cancer is a therapeutic option that could be considered in locally advanced stages. Unfortunately, no conclusive evidences are available with regard to the optimal sequence and timing of the different therapeutic strategies following radical surgery.

Material/Method: We retrospectively reviewed all patients discussed within the frame of our dedicated institutional multidisciplinary thyroid cancer tumor board. For the present analysis, we included only patients who received adjuvant external beam radiotherapy following radiometabolic therapy with 131-I, for T4 papillary thyroid carcinoma within the last 5 years. Only patients with at least 1-year of scheduled follow-up performed at our institution were eligible for statistical analysis. All patients were assessed by regular clinical evaluations, blood markers levels (thyroglobulin) and functional imaging with F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT). Adverse events were monitored according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.0.

Results: We collected data regarding 10 patients who received the full course of adjuvant external beam radiotherapy between 2017 and 2020. There was a male prevalence - 60% were male and 40% were female. The mean age was 63 years (range 44-78). The median time from surgical intervention to the start of the adjuvant external beam radiotherapy was 5 months (range 2-6). We used a conventional fractionation and the prescription dose 66 Gy to the tumor bed at patients with no evidence of residual disease, and 70 Gy for patients with evidence of residual disease on the functional imaging. Volumetric modulated arc therapy (VMAT) was performed. So far, all patients are still alive without any clinical or radiological evidence of local recurrence. Skin atrophy, oral mucositis and dysphagia were the most common reported side effects with 60% G1 and 40% G2. No G3 or higher toxicity were recorded.

Conclusions: Adjuvant external beam radiotherapy following radiometabolic therapy with 131-I for T4 papillary thyroid carcinoma is a feasible treatment option with acceptable toxicity rates. Longer follow-up time and larger series are desirable to draw more solid conclusions; however, a multidisciplinary discussion in high volume centers should be recommended to tailor the best treatment strategy.

P115

PREVENTION AND TREATMENT OF ORAL RADIATION-INDUCED MUCOSITIS IN HEAD AND NECK CANCERS: A REAL LIFE SURVEY AMONG 25 ITALIAN RADIATION ONCOLOGY CENTERS

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Aims: Radiation-related oral mucositis (OM) represents the most relevant dose-limiting side effect in head and neck cancer (H&N) patients (pts) treated with curative Radiotherapy (RT). Nevertheless, prevention and treatment of OM is not standardized, yet. Aim of the present survey was to investigate the daily clinical practice in preventing and treating OM among Italian Radiotherapy Centers.

Methods: Through a personnel contact, an online questionnaire, with multiple-choice and open-ended questions, was administered to 25 Italian Radiation Oncologists. The survey was composed of 4 sections: 1) center characteristics, 2) retrospective analysis of H&N pts treated in 2021 3) strategies to prevent OM 4) strategies to treat OM. All participants gave their consent to use the collected data for scientific purposes.

Results: All centers filled the proposed questionnaire. In 2021, a total number of 1414 pts (median pts/center = 54, IQR 20-70 pts, median pts' age = 65 years) were treated in the participating centers. The vast majority (92%) of them were submitted to IMRT and in 73% of them a concurrent platinum-based chemotherapy was also administered. The median value of median overall treatment time was 44 days (IQR 34-45) with a median of 3 days (IQR 0-5) interruption due to radiation-related toxicity. A median of 6% (IQR 3-15) of pts required enteral nutrition. The majority of centers collect pts' toxicity data at least once a week but only half of the centers have internal recommendations for the management of OM. Twelve centers (48%) did not use any agent to prevent OM while 13 centers use different strategies such as oral hygene, clorexidine, mixed mouthwashes, mucosa-adhesive films, ialuronic acid and antimicotic drugs. Similarly, OM is managed with different strategies according to the toxicity grade (Table 1).

Conclusions: A great heterogeneity exists among different centers in both prevention and treatment of OM in H&N cancer patients submitted to curative RT. Treatment interruptions and requirement of enteral nutrition due to radiation-related toxicity resulted quite limited suggesting that different strategies adopted to manage OM could be equally effective. Despite this, due to its relevant impact on the pts' compliance, further efforts should be pursued to minimize incidence and severity of OM to optimize the overall tolerance to RT.

Table 1. Topic and Systemic agents used in daily clinical practice.

Oral mucositis	Grade 1	Grade G2	Grade G3
	n. centers	n. centers	n. centers
Topic agents			
Bicarbonate	6	3	3
Hyaluronic acid	10	8	8
Antifungals	6	12	10
Antiacids	4	4	5
Benzydamine	3	5	4
Lidocaine	1	6	6
*Others**	10	10	7
Systemic agents			
Paracetamol	3	3	3
Steroids	2	5	11
Antifungals	-	8	18
Pain relievers	-	4	5
NSAIDs	1	5	4
Opioids	-	1	5
Antibiotics	-	1	4
*Others**	3	4	3

*Others**
Mucosite G1 topic: steroid, saline, vitamin E, LLT, honey, chamomile, calendula, chlorhexidine, gel and spray
Mucosite G1 systemic: food supplements, vitamin c, hyaluronic acid
Mucosite G2 topic: physiological solution, aloe vera, vitamin e, honey, chamomile, calendula, chlorhexidine, mucosyte, gel and spray
Mucosite G2 systemic: lidocaine, anitacids, electrolytes, vitamin c
Mucosite G3 topic: physiological solution, food supplements, equine catalase, honey, chamomile, calendula, mucosyte
Mucosite G3 systemic: antiacids, saline, lidocaine

P116

COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) AS A PREDICTOR OF TREATMENT OUTCOME IN ELDERLY HNSCC PATIENTS UNDERGOING RADIOTHERAPY

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Aims: To describe the role of CGA in predicting therapeutic and clinical outcomes such as treatment compliance and overall wellbeing through Frailty Index (FI) and therapeutic interventions.

Method: From July 2017 to December 2021 a total of 329 HNSCC pts were evaluated at our department, of which 36 refused RT or did the treatment elsewhere so 293pts were analyzed. From this pool: 114 <65yo; 58pts 65-70yo and 121>70yo. Initially, only pts >70yo had an oncogeriatric visit, but considering the multiple comorbidities that are frequent in HNSCC the age cut-off was

reduced to 65yo. So, prior to RT 91/179 (51%) elderly patients had a geriatric assessment, administered by an expert geriatrician, with the corresponding interventions on identified health issues. Treatment options were: CTRT, RT + Cetuximab or RT alone.

Results: Involved sites were: oral cavity 12; ipopharynx 5; larynx 19; oropharynx 47 [13 p16(-) and 31 p16(+) and 3 unknown p16 status]; different site 2 and nodal location 6 (3 unknown primaries; 3 neck relapses). After the geriatric visit, according to the FI 16 pts were considered fit, 54 pre-frail and 21 frail. 42pts (46%) received an intervention. 14/91, 19/91 and 58/91 pts underwent CTRT, RT+Cetuximab and RT alone (of which 5 palliative treatments).Of 58pts who underwent RT alone, 19 were considered frail; 34 pre-frail and 5 fit. In 26/58pts (45%) reduced volumes were given. A total of 88pts (97%) (20 frail, 52 prefrail and 16 fit) successfully completed the treatment. Among these pts 50 (57 %) (11 fit, 11 frail and 28 pre-frail) had nutritional support: oral supplements in 32pts, parenteral in 1 and enteral in 20. Some pts had a combined nutritional support. Only 9 (10%) (1 frail, 6 prefrail and 2 fit) were hospitalized. The most frequent G2/G3 adverse effects were dysphagia 41, mucositis 56 and dysgeusia 36. 7/88 (8%)pts died in the first three months after therapy; 4 pre-frail, 1 fit and 2 frail. 5 pts under RT alone and 2 under RT+Cetuximab. The cause of death was the deterioration of PS (4pts), acute renal failure (2pts) and pneumonia (1pt).

Conclusions: In our experience, the oncogeriatric visit was helpful in electing the vulnerable elderly patients, whom through various interventions complied better to the prescribed treatment. What comes to our attention is the fact that the pre-frail and frail category of FI are in need of major attention and the choice of treatment in these cases, must be through a multidisciplinary team.

P117

A SINGLE INSTITUTION EXPERIENCE OF THE RADIATION THERAPY ONCOLOGY GROUP (RTOG) 8502 "QUAD SHOT" REGIMEN FOR INCURABLE HEAD AND NECK CANCER (HNC)

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Aims: We report outcomes from palliative Radiation Therapy using QUAD shot regimen in elderly or frail patients (pts) with incurable head and neck cancer.

Method: From May 2021 to May 2022, twelve consecutive elderly or frail pts with incurable HNC were treated with at least one cycle of the RTOG 8502 regimen. Median pts age was 83 years (range 65-93) with Karnofsky Perfomance score from 60% to 80%. Pts had histologically confirmed head and neck carcinoma. All pts were ineligible for surgery, systemic chemoterapy or immunotherapy even as palliative care because of their age or frail conditions. Local symptoms from cancer mostly were pain and obstructive symptoms. Pts underwent computed tomography (CT)- simulation scans for planning QUAD shot RT. The gross tumor volume (GTV) identified through diagnostic images and physical examination, included only symptomatic disease. Clinical target volume was the same as GTV; 0,5 to 1.0 cm was added to GTV to create a planning target volume (PTV); 3,5 Gy /fraction twice a day, 6 hours apart, for 2 consecutive days, was prescribed to cover PTV, using 3-dimentional conformal RT or intensity modulated RT. 9 pts completed a cycle of QUAD shot regime (75%) and 3 pts completed a second cycle of QUAD shot regime (27%) after 3-4 weeks from the first treatment. For the second QUAD shot cycle, pts underwent a new CT-simulation scan to review PTVs and to take into account tumor response from previous QUAD shot cycle. Palliative response was defined as subjective relief of initial presenting symptoms through patient-reported outcomes in clinical notes.

Results: Tumor response was achieved in 9 pts (75%) and symptom relief in 7 pts (58%) of 12 pts. Overall response (tumor response or symptom relief) was achieved in 11 pts (92%). All pts who received 2 treatment cycles achieved overall response. Median overall survival (OS) was 5 months. Acute grade 2 mucosal and skin toxicity was observed in 2 pts (17%), no grade 3 was reported, no late toxicity was observed.

Conclusions: The favorable acute toxicity profile with rapid and durable palliation after RTOG 8502 "QUAD shot" regimen in the elderly or poor PS pts is clinically and logistically encouraging. Treatment with multiple cycles is recommended for better treatment response and/or survival. Our data has some limitations due to limited number of pts, further investigations with a collected larger number of pts is necessary to further validate the beneficial of this regime.

P118

"QUAD SHOT" REGIMEN USING IMRT FOR INCURABLE HEAD AND NECK CANCER (HNC)

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Aim: To review a single institutional experience of the Radiation Therapy Oncology Group (RTOG) 8502 "QUAD shot" regimen using IMRT IGRT for incurable head and neck cancer (HNC).

Matherials and Methods: From March 2021 to June 2022, we recruited ten consecutive patients with incura-

ble head and neck cancer (HNC), 3 females (30%) and 7 males (70%). Mean age was 80.5 (range 72-91) years. The performance status was established with the ECOG scale and the weight of each patient was recorded at the beginning and at the end of the radiotherapy cycle. All patients were treated with at least one cycle of the RTOG 8502 regimen. Treatment plans included the use of IMRT with 6 MV photons generated by a linear accelerator. Megavoltage cone beam (MVCB) was used for image-guided radiation therapy (IGRT). Two daily fractions of 3.7 Gy were delivered with an interval of at least 6 h for 2 consecutive days, totaling 14.8 Gy over 4 fractions. This was repeated every 3–4 weeks for a total of three cycles. No concurrent systemic therapy was performed.

Results: The number of completed cycles was 1 in 2 patients (20%) and 3 in 8 (80%). Tumor response was achieved in 8 (80%) patients and symptom relief in 10 (100%) patients. A total of 70 % of subjects had ECOG-2 and the others had ECOG -3. All patients who received two or more treatments cycles achieved overall response. Median overall survival (OS) was 5.7 months. Three (30%) patients died with median OS of 4 months; the others are all surviving today, with mean follow up of 6.4 months. The patients who died, were patients with ECOG-3. Body weight before and after radiotherapy course had an average increase of 2.36 kg (range 0-6.1 kg). Grade 1 toxicity was observed in 8 (80%) patients, but no acute Grade ≥ 1 or late toxicity was observed.

Conclusions: Our preliminary data are in agreement with those of the literature: the RTOG 8502 "QUAD shot" protocol using IMRT is efficacious and well tollereted for incurable HNC, with highly reduced toxicity. Treatment with multiple cycles is recommended for better treatment response and/or survival.

P119

18 FDG PET GUIDED HELICAL INTENSITY MODULATED RADIOTHERAPY IN LOCALLY ADVANCED NASOPHARYNGEAL CANCER: A MONO-INSTITUTIONAL EXPERIENCE

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Aim: Locally advanced nasopharyngeal cancers (NP) are usually treated with a combination of radiotherapy (RT) and chemotherapy (CT). Even if NP tumors, especially N2 or N3 disease, are associated with high distant metastasis rates, loco-regional control is crucial, as RT dose intensification demonstrated in last decades. Our aim was to assess clinical outcomes and toxicity after a dose intensified RT regimen in locally advanced NP.

Methods: From 2/2005 to 2/2021, 52 patients (pts) with NP (11 stage II, 16 stage III and 25 stage IV) were treated in our Center with Helical Intensity Modulated Radiation Therapy (IMRT). In 46 pts IMRT was delivered with a Simultaneous Integrated Boost (SIB) technique based on 18 FDG PET/CT, delivering 54 Gy (1.8 Gy/day) to the clinically negative neck region and 66 Gy (2.2 Gy/day) to tumor and positive nodal regions. In 19 pts a supplementary dose on PET positive volume to reach a total dose of 69 Gy (2.3 Gy/day) was delivered. Six pts, with a poorer performance status, received RT with a conventional fractionation: 50 Gy to the clinically negative neck region with a sequential boost on tumor and positive nodal regions up to 70 Gy. Twenty-six pts received neoadjuvant CT and 38 pts a concomitant platinum based CT. Toxicities were classified according to the CTCAE v5.0.

Results: Median follow–up was 63.3 months. The acute toxicity profile included: 10 G3 dermatitis, 11 G3 mucositis and 3 G3 dysphagia. Nine pts (11.5%) discontinued RT due to toxicity. Considering only the most relevant late toxicity, 3 hearing impairment, 1 G3 fibrosis and 1 temporal radionecrosis were reported, equally distributed between the various groups of pts. During the follow up period, 13 pts died (7 for cancer progression), 8 pts experienced a locoregional and 7 a metastatic progression. Six pts were lost. Overall Survival (OS) at 3 and 5-years was 85.6% and 77% respectively. Disease Free Survival (DFS) at 3 and 5-years was 71.9% and 68.5 % respectively. Even if DFS was significantly higher in stage II-III comparing to stage IV (p-value 0.005), there was not significant difference in OS between the two subgroups (p-value 0.453) (see Figure 1).

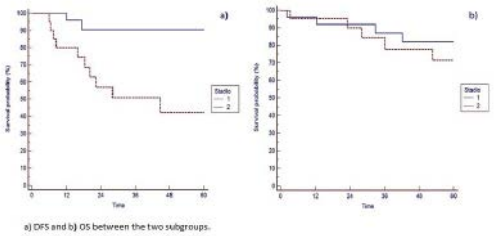

Figure 1.

Conclusions: With a long follow up period, survival rates are encouraging especially in Stage II or III. In our experience PET/CT guided dose intensification is feasible, with an acceptable toxicity profile. The comparison between 66 Gy and 69 Gy did not lead to a conclusive result and required further investigation.

P120

ASSESSMENT OF SARCOPENIA IN OROPHARYNGEAL CANCER PATIENTS TREATED WITH CURATIVE RADIOTHERAPY: TIME FOR A TAILORED APPROACH?

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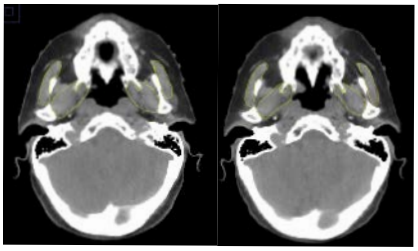
Aims: To identify sarcopenia and assess its impact on toxicities in a retrospective series of oropharyngeal cancer patients (pts) treated with curative Volumetric Modulated Arc Therapy (VMAT) +/- chemotherapy (ctx) at a single institution.

Methods: Oropharyngeal squamous cell carcinoma (SCC) pts who underwent curative radiotherapy (RT) +/- ctx at a single institution from 2010 to 2019 were considered for study inclusion. All pts received a 70 Gy/35fx RT and eventual ctx with 3 cycles of cisplatin every 3 weeks. Contouring of the cross-sectional area (CSA, cm^2) of the peri-mandibular masticatory muscles (CSA-MM) on both baseline (bl) and 60 Gy CT scans (Figure 1a) was performed. CSA-MM was used to estimate the CSA at 3th lumbar vertebra (L3) using the validated algorithm described by Chang et al. (2021) and was adjusted for pts height resulting in skeletal muscle index (M-SMI, cm^2/m^2). Sarcopenia was assessed with the relative cut-off proposed by Prado et al. (2008) and pts were divided into 3 subgroups (sarcopenic at bl, sarcopenic during RT, not sarcopenic).

Results: Among a total of more than 100 pts matching the inclusion criteria, we reported the preliminary results on a cohort of 32 pts (7 women, 25 men, median age 61 years - IQR 54-68); of them, 29 received ctx. According to TNM 7th edition, tumor stages were 15 stage III, 16 stage IVA, and 1 stage IVB, and 29 pts were p16+. Fourteen pts resulted sarcopenic at bl, while 9 sarcopenic during RT. In sarcopenic pts at bl a greater reduction in body mass index (BMI) at the end of RT and a greater number of grade (G) ≥ 2 mucositis during RT were reported. The neutrophil-lymphocyte ratio (NLR) was higher in sarcopenic pts at bl, as was its variation at the end of RT. The 66% of sarcopenic pts during RT had a Charlson Comorbidity Index (CCI) ≥ 5. Nutritional counselling during RT was activated in 64% of sarcopenic pts at bl and in 33% of sarcopenic pts during RT (Figure 1b).

Conclusions: Our preliminary data suggest that early identification of sarcopenia could bring additional information to aid clinical decision making i.e. the activation of a nutritional intervention to minimize toxicities and improve response to RT. Updated data from the whole cohort will hopefully lay the foundations for novel personalized approaches combining nutritional support and inflammatory biomarkers to minimize toxicity-related interruptions along RT or dose adjustment to improve oncological survival.



a

b

	Sarcopenic at baseline (n=14)	Sarcopenic during RT (n=9)	Not sarcopenic (n=9)	Whole cohort (n=32)
	n	*n*	*n*	*n*
BMI at baseline	26.2 (23.3-27.1)	27.3 (24.9-27.9)	25.9 (24.1–28.7)	26.2 (23.4–27.9)
BMI variation	-2.2 (-2.9– -1.6)	-1.7 (-2.6– -1.6)	-1.4 (-2.8– -1.3)	-1.9 (-2.8 – -1.4)
NLR at baseline	3.18 (2.56–3.95)	2.99 (2.6-3.5)	2.99 (1.95–3.81)	3.02 (2.12 –3.88)
NLR variation	10.3 (4.2–21.9)	13.9 (6.0-16.7)	7.2 (3.3-15.9)	10.7 (4.7–16.9)
Weight at baseline (kg)	81.0 (74.7–88.3)	87.0 (79.0-91.0)	74.0 (68.0–78.1)	79.5 (71.7–90.0)
Weight loss (kg)	-6.9 (-10.1– -5.1)	-6.0 (-8.4– -5.0)	-4.4 (-9.2– -3.6)	-6.4 (-9.2 – -4.1)
CCI-age adjusted ≥ 5	9 (64.3)	6 (66.7)	4 (44.4)	19 (59.4)
CCI-age adjusted < 5	5 (35.7)	3 (33.3)	5 (55.6)	13 (40.6)
Nutritional consulting during RT	9 (64.3)	3 (33.3)	3 (33.3)	15 (46.9)
Disphagia G ≥ 2	5 (35.7)	4 (44.4)	5 (55.5)	14 (43.7)
Mucositis G ≥ 2	8 (57.1)	4 (44.4)	4 (44.4)	16 (50.0)
Xerostomia G ≥ 2	2 (14.3)	1 (11.1)	2 (22.2)	5 (15.6)
Pain NRS ≥ 5	7 (50.0)	7 (77.8)	6 (66.7)	20 (62.5)

Figure 1. (a) ImageJ delineation of the masticatory muscles (threshold setting: -29 to +150 HU) at baseline (left) and 60Gy CT scan (right) in a patient sarcopenic during RT; (b) a summary of the main patients characteristics and toxicity outcome regarding the three subgroups and the whole cohort.

P121

VARIATIONS IN BODY MASS AND SKELETAL MUSCLE INDICES IN HEAD AND NECK CANCER PATIENTS UNDERGOING (CHEMO)RADIOTHERAPY AND NUTRITIONAL INTERVENTION

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Aims: We analysed a cohort of pat ients (pts) affected by head and neck squamous cell carcinoma (HNSCC), who underwent exclusive radiotherapy (RT) or concurrent chemo-radiotherapy (RT-CHT) to report the pattern of variation in their body mass (BMI) and skeletal muscle index (SMI).

Methods: Between 2016 and 2020, we analyzed the clinical records of 73 consecutive HNSCC pts treated by with definitive or post-operative RT (14 pts) or RT-CHT

(59 pts). All pts had nutritional evaluation at baseline and every three months during the follow up. In some cases, nutritional intervention with supplementation was necessary. At the time of diagnosis (t0) and 3 months after treatment completion (t3), CT scans were retrieved to measure skeletal muscle as the cross-section area (CSA) taken in a single slice at the level of C3 vertebra. Skeletal muscle area was defined as the pixel area between the radiodensity range of -29 and +150 Hounsfield Units (HU). We analyzed BMI and SMI at t0 and t3 for each patient. Charlson Score was used to assess comorbidities. Pts were followed-up to disease progression, relapse, or death. Progression free survival and differences among variables were evaluated by Wilcoxon signed-rank test.

Results: With a median follow-up of 16 months (range: 3-70 months), 9 disease progressions and 11 tumor relapses were observed. A total of 82% of pts was free from progression at 1 year (95% C.I. 0.70-0.89). At t0, average BMI was 25.8 (SD 4.1), while, at t3, it was 24.5 (SD 3.6) with a reduction in 54 pts (74.0%). The difference, evaluated with Wilcoxon signed-rank test, showed a BMI decrease of -1.3 (SD 1.8) with p-value <0.0001. At t0, average SMI was 57.1 (SD 11,01), while, at t3, it was 59.2 (SD 11.8) with a reduction in 26 pts (35.6%). The difference showed a SMI increase of 2.0 (SD 5.5) with p-value <0.0055.

Conclusions: SMI could represent a reliable and feasible tool for muscle mass assessment that could be easily integrated to monitor the nutritional status of the patients before, during and after treatment. According to our data, nutritional interventions and supplementation monitored by strict follow-up could lead to SMI stability or increment.

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CUNCURRENT SIB-IMRT PLUS CETUXIMAB IN LOCALLY ADVANCED SQUAMOUS CELL HEAD AND NECK CARCINOMA (LA-SCCHN) PATIENTS: A MULTICENTRIC EXPERIENCES IN DAILY CLINICAL PRACTICE

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Aims: To evaluate feasibility, toxicities and clinical outcomes (OR, LC and OS) in locally advanced squamous cell head and neck carcinoma (LA-SCCHN) patients unfit to receive platinum-based chemotherapy, treated with concurrent simultaneous integrated boost-intensity modulated radiotherapy (SIB-IMRT) and cetuximab in daily clinical practice.

Methods: From Jun 2014 to June 2022, we retrospectively selected all LASCCHN patients treated in a National multicentric study. Among these, 31 consecutive patients with LA-SCCHN submitted to SIB-IMRT plus Cetuximab have been selected and were included in this study. All patients had a life expectancy >6 months, Karnofsky Performance Status> 60 and adequate hematological/biochemical parameters including renal index.

Results: Data regarding 31 patients with squamous tumor were collected and reviewed. The primary tumor sites were: oropharynx in 15 patients (51.9%), oral cavity in 8 (25.9%), larynx in 4 (11%) and other sites in 4 (11%). There were 24 patients with T IV stage (19 stage T IVa and 5 stage T IVb). 27 patients had nodal involvement. Acute toxicities were observed in all treated patients (mainly mucositis, dermatitis and dysphagia) while 66.7% of patients developed late toxicities. All observed toxicities were grade 1 to 3 and just 1 patient developed a G4 toxicity (neutropenia). Complete response (CR) was observed in 66.7% of the patients, a partial response (PR) in 14.8% cases whilst 14.8% had a disease progression (DP). After 3 year of follow-up there were 8 deaths in the 31 patients studied, including 1 patient died for cardiovascular failure no treatment-related. The OS was 95.5%, 62.5% and 52.9% respectively at 1, 2 and 3 years follow-up.

Conclusions: Concomitant SIB-IMRT- cetuximab is an effective and safe treatment for patients with LA-SCCHN and can be used in real-life daily clinical practice.

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EXTERNAL AUDITORY CANAL TUMOR MANAGEMENT: A CASE REPORT AND PLAN COMPARISON

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Introduction/Aims: External auditory canal(EAC) cancer is a rare neoplasm, the squamous cell carcinoma(SCC) is the most common histology type. Given its rarity as well as peculiar location,the optimal treatment strategy is controversial. Definitive RT may be required when complete excision is not feasible. Data regarding the outcomes for cancer of the EAC with modern external beam RT are emerging, and the correct treatment planning is yet to be defined.We report a case of EAC cancer patient treated with IMRT. An insight into target delineation volumes, technical parameters, set-up choice, and a plan comparison with or without tailored

resin bolus is provided.

Methods: A 72 years old woman with intense pain and sudden bleeding from the EAC underwent a biopsy as the ENT assessed a suspicious lesion, then confirmed as a SCC. MRI and CT scan of the head and neck showed a subcutaneous lesion of 2 cm inseparable from the anterior wall of the right EAC extending medially for 9 mm, with reactive cervical lymph nodes (stage of disease cT1N0 Stell/Arriaga) Curative RT was prescribed over surgery, for a total dose of 69.96 Gy to the main lesion,59.4 Gy to the main microscopic spread sites including surrounding soft tissue, mastoid process, Eustachian tube (Chen,ROBPJ 2012) and 54 Gy to the ipsilateral elective nodes levels II,VIII,Xa (Vorwerk,ROJ2011; Gregoire 2013), for a total of 33 daily fractions. The challenges regarding dose calculation and preciseness of delivery inherent to the irregular surface led us to choose an intracavitary filling resin bolus in addition to the routine immobilization systems. Simulation CT scans were acquired with and without resin bolus for treatment planning decision. Two plans were separately calculated for comparison.

Results: Conformity Index (CI) and Homogeneity Index (HI) were calculated for all the ROIs in the two plans, showing better performance scores in both HI and CI for the target. PTV-T coverage was better met only when the resin bolus was used: V98≥98% of the prescribed dose, according to ICRU83 best recommendation. Toxicity profile was good after RT (only G≥2 erythema requiring topic therapy) with excellent resolution 50 days later (No G>1 CTCAE v5.0). Complete response both radiological and objective was assessed at first follow-up.

Conclusions: Modern RT for early-stage EAC is a valid option, despite robust evidence lacking. A tailored strategy involving resin bolus is recommended to avoid dose-calculation errors.

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FIRST EXPERIENCE ON ACUTE TOXICITY IN VMAT VERSUS 3D-CRT FOR LOCALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA AT IRCCS "CASA SOLLIEVO DELLA SOFFERENZA" OF SAN GIOVANNI ROTONDO

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Aims: The aim of this study is to assess retrospectively the acute toxicity in Volumetric Modulated Arc Therapy (VMAT) technique versus three-dimensional conformal radiotherapy technique (3D-CRT) for locally advanced head and neck squamous cell carcinoma (LAHNSCC) in post-operative and curative setting during radiotherapy (RT) treatment.

Methods: One hundred thirty nine consecutive patients (pts) with LAHNSCC were treated in our department. Seventy one pts before 2018 were treated with 3D-CRT technique, and 68 pts after 2018 were treated with VMAT technique. Fourty eight pts underwent to definitive (24 pts each in VMAT group and 3D-CRT group) and 91 pts to post-operative RT (44 and 47 pts in VMAT and 3D-CRT group, respectively). The median dose was: 70 Gy/35 fractions (VMAT group) and 66 Gy/33 fractions (3D-CRT group) for definitive treatment; 66 Gy/33 fractions (VMAT group) and 60 Gy/30 fractions (3D-CRT group) for post-operative treatment.

Results: During RT treatment VMAT toxicity pattern in 68 pts and 3D-CRT in 71 pts was noted down. Acute toxicities were reported according to RTOG score, and the comparison between 3D-CRT vs VMAT was made with Chi square test or Fisher's exact test. Overall acute grade 2 toxicity was significantly lower in the VMAT group, while acute grade 3 toxicity was higher in the 3D-CRT group, but not statistically significant. Pts underwent to definitive RT (24 pts) developed a significant lower grade 2 toxicity in the VMAT group than in the 3D-CRT group: grade 2 acute toxicity skin occurred in 8 of 24 (33.33%) pts in the VMAT group and in 16 of 24 (66,67%) pts in the 3D-CRT group (p=0.042); grade 2 acute mucositis occurred in 6 of 24 (25%) pts in the VMAT group and in 14 of 24 (58.33%) pts in the 3D-CRT group (p=0.039); grade 2 acute dysphagia occurred in 4 of 24 (16.67%) pts in the VMAT group and in 11 of 24 (45.83%) pts in the 3D-CRT group (p=0.05). In adjuvant setting (91 pts) 12 of 44 (27.27%) pts in the VMAT group developed grade 2 skin toxicity compared with 25 of 47 (53.19%) pts in the 3D-CRT group (p=0.021). No significant difference about mucositis and dysphagia was recorded between the two treatment groups.

Conclusions: In our analysis VMAT technique provided less acute toxicity in pts treated for LAHNSCC than the 3D-CRT technique. Statistically significant higher acute toxicity were reported in pts underwent definitive RT.

P125

EFFECTS OF RADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED ORAL CANCER WITH FLAP RECONSTRUCTION

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Aims: Locally advanced oral cavity cancer (LAOC) is a highly morbid disease, often characterized by a functional decline caused by both tumour progression and treatment effects. Surgical management of LAOC requires radical resection (with clear margins of at least 1 cm) as a result, large and complex tissue defects are often performed, needing surgery reconstruction with local, regional or free flap. Since adjuvant radiotherapy (RT) is often needed, our aim is to evaluate the effects of RT in patients who underwent flap reconstruction, in terms of local disease control, functional outcomes and patients' quality of life (QoL).

Table 1.

Characteristics		Percentage
Sex	Males	66.66%
	Females	33.33%
Age	<55 y.o.	20.83%
	55-64 y.o.	33.33%
	65-74 y.o.	33.33%
	>75 y.o.	12.50%
Comorbidities	None	33.33%
	Diabetes	16.66%
	Hypertension	37.50%
	Hypercholesterolemia	12.50%
Localization	Tongue	29.16%
	Floor of the mouth	20.83%
	Buccal mucosa	33.33%
	Mandibular gingiva	16.66%
Stage	T2 any N	33.33%
	T3 any N	37.50%
	T4 any N	29.16%

Table 2.

Treatment		Percentage
Chemotherapy schemes	None	58.33%
	Concomitant cisplatin	41.67%
Radiotherapy schedules	200-6400 cGy to oral cavity 200-5200 cGy to lymph nodes	45.82%
	210-6090 cGy to oral cavity 180-5220 cGy to lymph nodes	33.33%
	220-6600 cGy to oral cavity 175-5250 to lymph nodes	20.83%

Method: From 2019 to 2022, at University of Catania 24 patients affected by LAOC have been enrolled (Table 1). All patients performed both surgery and reconstruction followed by radiotherapy (64-66 Gy in 30-32 Fx to oral cavity, 52-52,50 Gy in 26-30 Fx to neck lymph nodes) with or without concomitant chemotherapy (CT) with cisplatin (Table 2). The most used flaps have been free vascularized tissues, which are resistant to ionizing radiation and help avoid suboptimal outcomes and higher complications. All patients have been radiologically evaluated through head and neck TC scan, both before and after 6-8 weeks the end of adjuvant therapies; moreover, all patients have been clinically evaluated during all the treatment course and at trimestral follow-up.

Results: During the adjuvant treatment course, the most performed adverse effects have been G1-G2 G.I. toxicities, such as dysphagia, dry mouth and mucositis (62.50%), followed by G2-3 cutaneous and G.I. toxicities (16.66% and 12.50% respectively). Both during and after radiotherapy, none of the patients performed moderate or severe sequels, such as severe dehiscence, exposed bone/graft, orocutaneous fistula, or flap loss, requiring surgery. Local disease control rates have been 78%.

Conclusions: Adjuvant radiotherapy after flap reconstruction in patients affected by LAOC remains one of the most challenging problems in head and neck oncology. Even if longer follow-up period and further investigations are needed, to date it can be concluded that radiation therapy does not predispose patients to more frequent or severe surgical complications following flap reconstructive surgery.

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IMRT TREATED HEAD AND NECK CANCER PATIENTS' CLINICAL OUTCOME AND QUALITY OF LIFE: OUR EXPERIENCE OF DATA RECOLLECTION AND ANALYSIS

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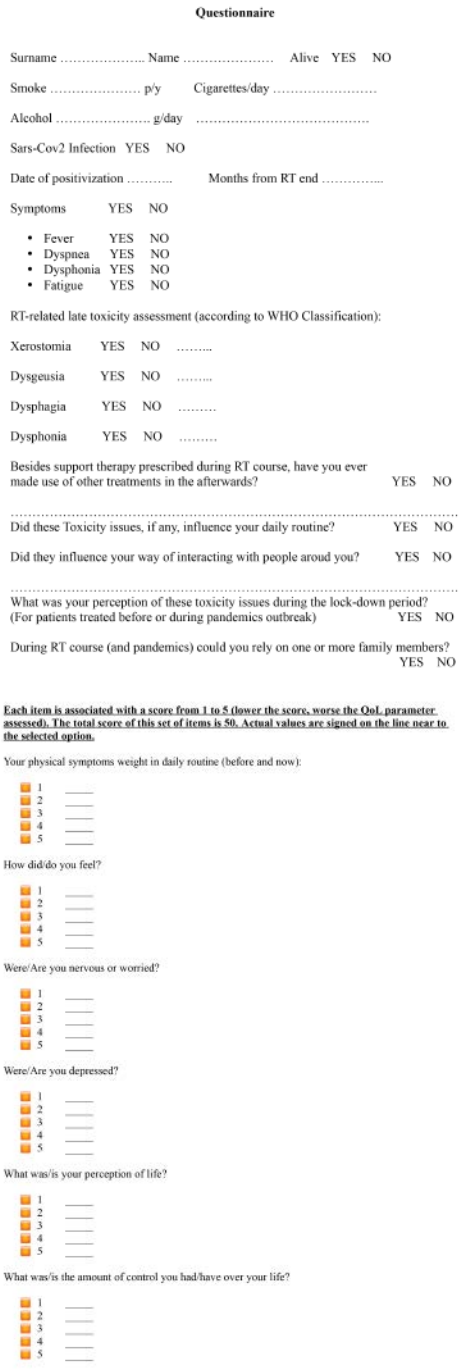
Aims: Looking back to the patients (pts) we treated with IMRT during the past 3 years, we decided to make an assessment of their overall survival (OS), progression free survival (PFS) and late toxicity. Furthermore, a quality of life (QoL) comparative analysis of before and after treatment was performed, trying to determine the actual weight of RT, comparing it with surgery's.

Method: A retrospective series of pts with Head and Neck cancers, who underwent exclusive IMRT or concomitant CTRT (depending on the tumor stage), in the past 3 years, were enrolled. Updated follow up (FU) data were acquired by phone, administering a questionnaire we made, using McGill's one (2019) for QoL assessment as basis. Each toxicity parameter was measured according to the RTOG/EORTC criteria.

Results: A total of 54 pts, with median age at diagnosis of 67 years (range 50-87 years) were enrolled. Median FU period was 18 months (range 7-40 months). Crude rates of PFS and OS respectively were 75% and 76%. Each patient was reassessed through radiological and functional imaging at 6 and 12 months after treatment. Local and distant recurrence rates respectively were 23% and 2%. Late toxicity was found in 29 pts (54%) with it being classified, according to RTOG/EORTC criteria, as "moderate"/G2 in 8 (15%) of them. 4 pts (7%) reported a general improvement of their QoL after RT. 28 pts (52%) reported late toxicity influenced their daily life and interactions with other people, resulting in a QoL worsening. 17 of them (61%) reported their QoL worsening was mostly influenced by previous surgery, with 82% of them undergoing total laryngectomy. This observation con-

firms an inferior QoL in pts submitted to radical surgery. 13 pts (24%) were treated before 2020 with consequential FU interruption during the lockdown period. 6 of them (11%) reported an aggravation of RT-related toxicity, with later improvement after the removal of restrictions.



Questionnaire

Surname …….. Name …….. Alive YES NO

Smoke …….. p/y Cigarettes/day ……..

Alcohol …….. g/day ……..

Sars-Cov2 Infection YES NO

Date of positivization …….. Months from RT end ……..

Symptoms YES NO

- Fever YES NO
- Dyspnea YES NO
- Dysphonia YES NO
- Fatigue YES NO

RT-related late toxicity assessment (according to WHO Classification):

Xerostomia YES NO ……..

Dysgeusia YES NO ……..

Dysphagia YES NO ……..

Dysphonia YES NO ……..

Besides support therapy prescribed during RT course, have you ever made use of other treatments in the afterwards? YES NO

……

Did these Toxicity issues, if any, influence your daily routine? YES NO

Did they influence your way of interacting with people aroud you? YES NO

……

What was your perception of these toxicity issues during the lock-down period? (For patients treated before or during pandemics outbreak) YES NO

During RT course (and pandemics) could you rely on one or more family members? YES NO

Each item is associated with a score from 1 to 5 (lower the score, worse the QoL parameter assessed). The total score of this set of items is 50. Actual values are signed on the line near to the selected option.

Your physical symptoms weight in daily routine (before and now):

1 ____
2 ____
3 ____
4 ____
5 ____

How did/do you feel?

1 ____
2 ____
3 ____
4 ____
5 ____

Were/Are you nervous or worried?

1 ____
2 ____
3 ____
4 ____
5 ____

Were/Are you depressed?

1 ____
2 ____
3 ____
4 ____
5 ____

What was/is your perception of life?

1 ____
2 ____
3 ____
4 ____
5 ____

What was/is the amount of control you had/have over your life?

1 ____
2 ____
3 ____
4 ____
5 ____

How did/do you feel, thinking about the future?

1 ____
2 ____
3 ____
4 ____
5 ____

How was/is your memory? Did/do you have difficulties remembering things?

1 ____
2 ____
3 ____
4 ____
5 ____

How did/do you feel your relationships and communications with people around you were/are?

1 ____
2 ____
3 ____
4 ____
5 ____

How do you think your condition affected/affects people around you?

1 ____
2 ____
3 ____
4 ____
5 ____

Conclusions: Despite pandemic and pts residing elsewhere, we were able to collect all the data we needed in order to make a complete assessment. When contacted, most of the pts reported no symptoms (G0) or mild late toxicity issues (G1). This could be partially related to the prescription of a support therapy at the beginning of RT. Previous surgery (especially radical one for larynx cancer) and pandemic's psychological impact respectively proved to be meaningful in terms of pts' QoL and their perception of RT-related toxicities.

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ADJUVANT RADIOTHERAPY IN GIANT HEAD AND NECK HEMANGIOPERICYTOMA: A CASE-REPORT

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Aims: To assess efficacy and tolerance of adjuvant radiation treatment (RT) in a patient affected by a giant head and neck-hemangiopericytoma (H&N-HPC) with surgical positive margin. HPCs are rare tumors that arise from pericites, develop in deep soft tissues, especially those of extremities or retroperitoneum and generally affects middle-age patients. About 15-30% of all HPCs occurs in head and neck regions. The mainstay of treatment is radical surgery with wide excision margins and there are no clear guidelines for adjuvant treatments due to the rarity of the disease.

Methods: This study shows a case-report of 42-year-old man, affected by a giant (9 cm of diameter) HPC of the base of tongue, who had undergone two surgical approaches to remove the bulky tumor and the residual disease. The last surgery showed a deep positive margin (R1). Therefore, adjuvant RT was prescribed. The Clinical Target Volume (CTV) was tumor bed with subclinical extension and the Planning Target volume (PTV) was generated adding 5 mm of margin to CTV in all directions.

The total dose of 66 Gy in 33 fractions was prescribed to PTV. The technique used was VMAT with daily IGRT-Cone Beam CT (CBCT). The patient was seen twice a week during treatment and for follow-up visits 2 months after completion of treatment, then four month' interval with otolaryngological visits, neck MRI and/or PET. Acute and long-term toxicities were verified according to CTCAE v5.0 staging system.

Results: The patient did not show toxicities during the first part of treatment, but experienced G2 mucositis and G1 skin toxicity (dermatitis) toward the end of the treatment, without treatment interruption. First follow-up at 2 mouths from the end of RT showed no mucositis, mild soft tissue edema, and xerostomia G1. At 12 months of follow-up, there was no clinical or radiological evidence of recurrence. Patient shows only mild toxicity due to xerostomia G1.

Conclusions: The role of RT in the H&N-HPC is still controversial due to the limited data available in literature. However, RT could play a role in the multi-modal management of these patients especially in the cases of non-radical surgery and/or in presence of other risk factors, after multidisciplinary discussion. Patient is NED (no evidence of disease) one year after RT with low toxicities. However, a long-term follow-up is required due to the uncertain behavior of this tumor.

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RADIOTHERAPY FOR KAPOSI'S SARCOMA. A CASE REPORT

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Aims: Kaposi Sarcoma (KS) is AIDS related neoplasm, although its incidence has declined. Non AIDS related KS is uncommon disease and often it hasn't clinical importance. Radiotherapy represents an effective palliative treatment for bleeding and edema, due to KS radiosensitivity. The treatment for each patient needs to be individualized. Side effects are rare, with minimal skin reactions, except for mucosal lesions.

Methods: We report a case of a 87-year-old man affected by classic non AIDS related KS involving the oropharynx (right tonsil), who was found to have a biopsy proven KS lesion. Level IB-II bilateral lymph nodes were metastastic at imaging (MRI). Ki-67 Proliferation index was 25-30%. No systemic therapies had been given. Patient referred local pain, dysphagia, and bleeding. TC simulation and thermoplastic head mask was performed. The treatment was delivered by Volumetric Modulated Arc Therapy (VMAT) technique with 6 MV photons. Prescribed dose was 40 Gy in 20 daily fraction to Planning Target Volume (PTV), which includes right tonsil and ipsilateral neck, both with adequate margins. Cone-Beam CT and ExacTrac system from Brainlab was adopted for set-up position control. A clinical examination every 10 Gy was planned to evaluate treatment tolerance.

Results: At first after 10 Gy, and then at 20 Gy, no relevant toxicity was report. RT was well tolerated and limited side effects were observed. After 20 Gy, there was resolution of bleeding and pain, for which the patient decided to suspend the RT. At the clinical check-up after about 3 months to the end of treatment, the clinical examination showed a complete response at the level of the tonsil but not for the nodes. At 12 months to the end of treatment MRI detected complete response.

Conclusions: We reported a case of a rare KS with an uncommon onset site. RT could be considered an effective and safe treatment option and played a crucial role to achieve a local control of pain, dysphagia and bleeding, without relevant side effects. The case is a good representation that clinical efficacy on primary cancer is achieved even with low dosage.

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BEVACIZUMAB FOR RADIATION NECROSIS FOLLOWING STEREOCTACTIC RADIOTHERAPY OF NON SMALL CELL LUNG CANCER BRAIN METASTATIC DISEASE

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Aims: Bevacizumab (BV), an anti-vascular endothelial growth factor monoclonal antibody, has been increasingly used for the treatment of radionecrosis (RN) after stereoctactic radiotherapy (SRS) for brain metastasis. The aim of our study was to evaluate the efficacy and safety of bevacizumab for treatment of RN in patients (pts) affected by non-small cell lung cancer (NSCLC) brain metastases (BM) treated with stereotactic radiotherapy (SRS).

Method: Between July 2011 and October 2021, a total of 121 pts (median age 67, M: F 1,5: 1) presenting with 187 metastases were submitted to SRS. All of them had KPS ≥70. Gross tumor volume (GTV) was defined as macroscopic contrast enhancing lesion on T1-MRI. Planning tumor volume was obtained by adding to GTV an isotropic margin of 3 mm in all directions. The RT treatment was carried out using True Beam LINAC VARIAN System, 6MV photons. We utilized a head thermoplastic mask as immobilization system Radiological

response on MRI was assessed by a neuroradiologist according to the RANO-BM criteria. Brain progression-free survival (BPFS) and Overall Survival (OS) rates from the diagnosis of BM were calculated from the date of first radiotherapy treatment using the Kaplan-Meier method. In this analysis we evaluated results in terms of radiation-induced brain necrosis, trying to find a correlation with the delivered dose and the planning volume.

Results: Median overall survival (OS) was 7,6 months (CI 7.4-10.8). Seventy-one pts developed radiation-induced brain necrosis as documented by the subsequent MRI. This reaction was not statistically related to GTV-volume(p=0,350) but was related to high BED 10 and BED 12(p=0,054) The patients with RN treated with bevacizumab had an increase in OS (p = 0.020; HR 0.332; RC -1.103).

Conclusions: BV presents a promising treatment strategy for patients with RN and brain metastatic disease. Radiographic response, clinical and OS improvement was observed without any serious adverse events.

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STEREOTACTIC BODY RADIOTHERAPY IN OLIGO-PROGRESSING METASTATIC LUNG CANCER, A VALUABLE TREATMENT?

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Aims: Oligoprogression (OPD) is defined as a condition characterized by a limited progression (1-3 metastases) observed in patients undergoing systemic cancer treatment. Local treatment of OPD might delay systemic therapy line switch, which could be beneficial in patients with prolonged global disease control due to novel targeted or immune therapies. Tha aim of our study was the evaluation of the impact on outcome of stereotactic body radiotherapy (SBRT) in patients with OPD from metastatic lung cancer.

Method: We collected data from a cohort of consecutive patients treated with Cyberknife and Linac-based SBRT between June 2015 and August 2021. All extracranial metastatic sites of OPD from lung cancer were included. Dose regimens consisted of 24 in 2 fractions, 30-51 Gy in 3 fractions, 30-55 Gy in 5 fractions, 52.5 Gy in 7 fractions and 44-56 Gy in 8 fractions. Dose was expressed as Biological Effective Dose for α/β=10 (BED10). Kaplan-Meyer method was used to calculate Overall Survival (OS), Local Control (LC) and Disease Free Survival (DFS) from the start date of SBRT to event.

Results: Sixty-three patients, 34 female and 29 male were included, with a median age of 75 years (range 25–83). All patients undergoing concurrent systemic treatment before the start of the SBRT: 19 chemotherapy (CT) alone (30%), 26 CT plus immunotherapy (IT) or plus Tyrosin kinase inhibitors (TKI) (41%) and 18 IT/TKI alone (29%). SBRT was delivered to lung (n=29), mediastinal node (n=9), bone (n=7), adrenal gland (n=19), other visceral metastases (1) and other node metastases (n=4). A median BED10 of 104 (range 39-151) Gy10 was delivered. Median Overall Survival was 23 months after a median follow up of 20 months (range 1-48) (Figure 1). LC was 93% at 1 year and 87% at 2 years. DFS was 7 months. At univariate and multivariate analysis any (age, type of systemic treatment, metastatic site receiving SBRT and BED) statistically significant prognostic factor for patients with oligoprogression SBRT treated was found for overall survival.

Conclusions: SBRT in patients with oligoprogressing lung cancer resulted in a long median OS of 23 months. One-year LC was 93% and median DFS was 7 months. SBRT may allow to continuate an effective systemic treatment as other metastases grow slowly. SBRT could be a valide option to postpone the change of chemotherapy and/or immunotherapy. More research is needed to select OPD patients eligible for SBRT.

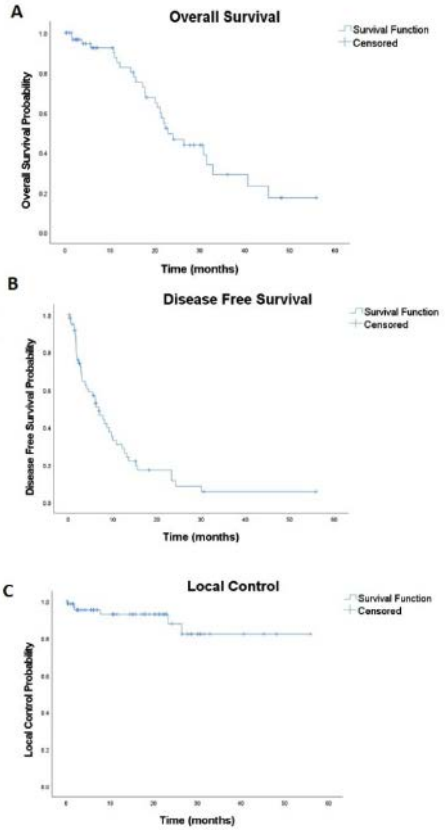

Figure 1.

P131

THE ROLE OF AGATSTON SCORE AND CARDIAC DISEASE IN NON SMALL CELL LUNG CANCER PATIENTS

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Aims: Radiation-induced cardiac toxicity and radiation-related coronary artery disease (CAD) represent an important issue in thoracic radiotherapy, although no reliable surrogate biomarker are identified. The history of previous cardiac functionality and the quantification of coronary calcium based on the area of a calcified coronary plaque in a CT slice is called Agatston score, or Coronary Artery Calcification Score (CAC Score) and could represent a potential biomarker for radiation-induced cardiac toxicity. The aim of our work is to evaluate the prevalence and severity of cardiac calcifications in lung cancer patients.

Method: Between January 2018 and May 2022, patients non-small cell lung cancer (NSCLC) with a pretreatment CT imaging of the thorax that were discussed in the Multidisciplinary Tumor Board (MTB) of thoracic malignancies in our Department were included. The clinical data of the patients were retrospectively collected (sex, age, smoke exposure, stage, cardiac disease) and Agatston score was calculated on CT imaging and was correlated with the clinical parameters (Chi-Square analysis) and with overall survival (OS, with Kaplan-Meier analysis).

Results: A total of 167 patients were included in the present analysis, , with a median OS of 15 months (mean 19,2 months, 95% CI 12-36 months). The four CAD Score subgroups differed in terms of sex (p<0,001), age (p<0,001), smoke exposure (p<0,001), hypertension (p<0,001), cardiac disease (p<0,001). The parameters that resulted significantly correlated with a lower OS were the Stage (p<0,001), the CAD Grading (p:0,001) and previous cardiac disease (p:0,001).

Conclusions: The prevalence of severe CAC Grading is exceedingly high in lung cancer patients at all stages of disease, that are amenable to undergo different treatments. Patients with severe CAC grading as well as previous cardiac disease, independently from the choice of treatment, should always be referred to the Cardiologist for prevention and strict follow up of CAD.

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TOXICITY PROFILE AND FEASIBILITY OF CONSOLIDATION RADIOTHERAPY, CONCOMITANT OR NOT WITH WITH ATEZOLIZUMAB, IN PATIENTS WITH SCLC- EXTENSIVE STAGE AFTER FIRST LINE OF CHEMOTHERAPY

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Aims: To investigate the treatment toxicity and feasibility of consolidative thoracic radiotherapy (RT) (based on CREST Trial: 30 Gy/10 fractions), concomitant or sequential, with Atezolizumab mantenaince in Small Cell Lung Cancer - Extensive Stage (SCLC-ES) patients with residual thoracic disease after first line therapy.

Methods: We retrospectively collected datas on 21 patients (pts) with SCLC-ES from February 2021 to June 2022 treated at our Radiotherapy Unit. The weighted median age was 63 years (57% male), with good KPS, former smokers. Patients were divided in two groups, group A (8 pts, consolidation RT and sequentially Atezolizumab mantenaince) and group B (13 pts, consolidation RT concomitant to Atezolizumab). In the first group were included elderly patients or subjects who complain fatigue or KPS decreasing during first line chemotherapy. Clinical toxicity (bronchopulmonary and esophageal) was reported by clinician evaluation and patients report.

Results: No difference beetwen groups was detected in rates of grade ≥3 pulmonary toxicity (0% of pts), instead esophageal toxicity (grade > 3) was 7.6% in group B and 0% in the group A. The dysphagia, oromucositis and consequent weight loss, persist after RT consolidation course.

Conclusions: Results from this retrospective study, although of small size, suggest that consolidation radiotherapy is safe and well tolerated in both setting (concomitant or sequential). Further evidences from larger samples are needed to confirm our findings, but longer follow-up with regard to tumour control certainly indicate the best therapeutic strategy in the SCLC-ES.

P133

STEREOTACTIC ABLATIVE RADIOTHERAPY AND DURVALUMAB: THE BACKBONE OF UNRESECTABLE LOCALLY ADVANCED NON SMALL CELL LUNG CANCER PATIENTS UNFIT TO CONCURRENT CHEMO-RADIOTHERAPY

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Aims: In Europe, the standard of care for fit unresectable locally advanced non-small cell lung cancer (LA-NSCLC) PD-L1 >1% patients is concurrent chemo-radiotherapy (ChT-RT) followed by Durvalumab. Several real world experiences have been reported about safety and effectiveness of Durvalumab after concurrent or sequential ChT-RT. There is a lack of data after sequential ChT-hypofractionated RT. Unresectable LA-NSCLC patients who were unfit for concurrent ChT-RT were enrolled in a non-randomized, single arm, single institution phase II trial (Clinical trials.gov NCT05291780). We report safety and effectiveness of stereotactic ablative radiotherapy (SABR) in LA-NSCLC patients treated with radical-intent based on PACIFIC trial.

Methods: Neoadjuvant ChT (3-4 cycles) was administered before SABR. The gross tumor volume (GTV) included primary tumor (GTV-T) and CT-PET positive node/s (GTV-N). Patients who had not progression of disease after neoadjuvant ChT and SABR, received Durvalumab as consolidation therapy every two weeks for up to 24 cycles or until progression or unacceptable toxicity in patients enrolled in expanded access program.

Results: Between June 2015 and May 2022, 12 LA-NSCLC PDL-1 >1% patients unfit for concurrent ChT-RT were enrolled. Cancer stage was IIIA and IIIB in 4 and 8 pts; 6 and 6 had adenocarcinoma (ADK) and squamous cell carcinoma (SCC), respectively. All cases had PTV overlapping the major airways. Median prescribed dose was 45 Gy (range, 40-55) and 40 Gy (35-45) in 5 fractions to T and N, respectively. Median follow-up achieved 16 months (range, 4-55). Today, 3 (30%) patients are still in treatment and 4 (40%) completed 24 cycles of immunotherapy. Three (25%) and 2 (16%) patient had experienced local recurrence (LR) and distant metastasis (brain and lung) during consolidation therapy; of these 4 discontinued Durvalumab after a median time of 9 months (range, 8-10) after SABR and 1 received SABR to oligoprogressive site and continued Durvalumab to completion. One (8%) developed LR 30 months after completing treatment. At last follow-up 10/12 (83%) patients were alive, 3 (25%) started ChT after LR. The median duration of Durvalumab was 10 months (range, 4-24) for all patients and 12 months (range, 4-24) for patients who had not disease progression. One (8%) patient experienced ≥G3 esophageal toxicity 4 months after SABR and discontinued Durvalumab.

Conclusions: PACIFIC trial has revolutionized the management of LA-NSCLC. SABR and immunotherapy could be the backbone of patients unfit to concurrent ChT-RT.

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THORACIC RADIOTHERAPY AND TYROSINE KINASE INHIBITORS ASSOCIATION: PRELIMINARY RESULTS FROM A MONOINSTITUTIONAL EXPERIENCE

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Aims: In Epidermal Grow Factor Receptor (EGFR) mutant non-small-cell lung cancer (NSCLC), local radiotherapy (RT) has become a new standard of care, improving survival. Furthermore, TKIs have radiosensitizing effects, but combined with consolidation thoracic RT might cause an impairment of normal lung function, due to possible toxicity arising from their combination. This leads, in clinical practice, to stop TKIs when RT in ongoing. As few data are available in this therapeutic setting, we evaluated the feasibility and tolerance of Intensity Modulated RT (IMRT) delivered by means of Helical Tomotherapy (HT) or Stereotactic Body Radiotherapy (SBRT) delivered by Cyberknife (CK) in pts with EGFR mutant NSCLC under TKIs treatment.

Methods: Between April 2017 and January 2022, 18 patients (pts) with stage IV NSCLC treated with concomitant RT (60-62.5 Gy/25-30 fractions for IMRT and 40-60 Gy/3-8 fractions for SBRT) and TKIs were evaluated retrospectively. Our main endpoint was lung toxicity, while overall survival (OS) was secondarily described. Post-treatment scans (TC or PET) were used to evaluate local response, using the RECIST criteria, and radiological toxicity. Acute toxicity was assessed according to the CTCAE v5.0. Survival curves were calculated from the date of treatment by using the Kaplan-Meier method.

Results: Median age of the pts at the time of RT was 69.4 years (45.4-83.6). Median follow up (FU) was 16.81 months (0.5-51.87). Median time occurring between start of TKIs and beginning of RT was 9.39 months (1.12-71.07). Treatments were delivered with HT (14/18) and CK (4/18). The mean PTV was 114.92cc (8.69-379.5 cc). Mean lung Equivalent Dose in 2 Gy was 12.4 Gy (7.2-

21.1 Gy). TKIs administrated were Osimertinib (9/18), Erlotinib (4/18), Gefitinib (3/18) and Afatinib (2/18). Median OS was 37.1 months. At 3 and 6 months FU, radiological toxicities were respectively 67% and 39% among all pts; at first FU 75% (9/12) G1 and 25% (3/12) G2. No G3 radiological toxicity was recorded nor clinical, while 3/12 pts experienced G1 clinical toxicity needing supportive care (antibiotics or steroids). At 6 months, 6 pts showed G1 radiological toxicity and 1 pt G2, but all were clinical G0.

Conclusions: Our findings shows that the association between thoracic radiotherapy and the administration of TKIs is a safe and well tolerated treatment scheme. The analysis of a larger sample size and a longer clinical follow-up are needed to confirm these preliminary results.

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STEREOTACTIC BODY RADIOTHERAPY FOR ELDERLY LUNG CANCER PATIENTS: RESULTS OF MONO-INSTITUTIONAL EXPERIENCE

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Aim: This study aims to evaluate retrospectively the efficacy and safety of stereotactic body radiotherapy (SBRT) in elderly patients (pts) with lung cancer, in early and advanced (metastatic) or oligoprogressive disease.

Methods: From February 2018 to March 2022, 69 pts, aged more than seventy years old and affected by lung cancer, have undergone to SBRT technique in our Center by means of Cyber Knife® (Accuray, Sunnyvale, CA) (CK). Median age was 79, 41 (70-92,53), 47 pts were at stage IV and 22 at stage I. Eighty-eight lesions were treated and were stratified by histological diagnosis: (42) Adenocarcinoma, (3) Neuroendocrine carcinoma, (13) Squamous cell carcinoma, (5) Small cell lung cancer and (25) unknown since biopsy was not possible because of the patients' performance status. Previous chemotherapy, surgery or radiation therapy were not exclusion criteria. The different fractioned regimens depend on tumor site and diameter: 30-60 Gy in 1-8 fractions; Median Equivalent Dose in 2 Gy (EQD2) was 96.875 Gy (83.33-126 Gy). Median prescription isodose was 80% (70-84%) and median PTV was 18.45 cc (1.61-72.46 cc). Among all pts, six received concomitant systemic therapy according to international guidelines. Outcomes of interest included rates of local control (LC), defined on Computer Tomography or PET-FDG according RECIST criteria, as well as treatment-related toxicity scored by CTCAE v5.0.

Results: The median follow up was 42.3 months and four pts were lost. All pts concluded SBRT without acute toxicity events and no significant late toxicity were observed. Only one patient, after six months, exhibited radiation pneumonitis, without symptoms. Among the lesions treated, twenty-nine presented partial response and forty presented complete response. Overall Survival (OS) was 80% at 6 months, 72% at 12 months, 65.3% at 24 months. LC rate was 86% at 6 months, 79% at 12 months and 59 % at 24 months (Figure 1). Moreover, there were not a statistical significant correlation in LC and in OS between the two TNM stages. By performing a multivariate analysis and dividing the pts by stage and histology, no significant difference was found in OS and LC.

Conclusions: Our preliminary results show that SBRT with CK should be considered as treatment strategy in elderly pts affected by lung cancer. The risk of serious adverse events was acceptable and the treatment is well tolerated. Further investigation is necessary in order to have long term results and larger series.

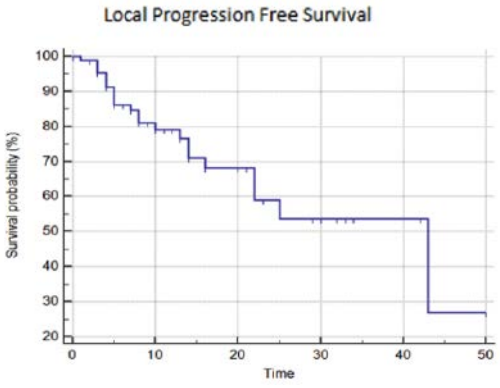

Figure 1.

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EXTENSIVE-STAGE SMALL CELL LUNG CANCER IN THE IMMUNOTHERAPY ERA: WHICH IS THE ROLE OF CONSOLIDATIVE THORACIC RADIOTHERAPY?

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Aims: Extensive stage small cell lung cancer (ES-

SCLC) is still characterized by a poor prognosis. The recent introduction of concurrent immunotherapy (IT) seemed to obtain better outcomes without increasing toxicities. Conversely, the role of thoracic radiotherapy (TRT) is still largely debated in this setting. The aim of this study is to evaluate clinical outcomes and safety of consolidative TRT in ES-SCLC patients (pts) receiving concomitant chemo-immunotherapy (CT-IT).

Method: We conducted a monocentric retrospective analysis on 33 pts affected by ES-SCLC (defined as metastatic or locally advanced SCLC not suitable for upfront radical concomitant CT-RT) initially treated with first line CT-IT from February 2020 to May 2022. Main pts features are summarized in Table 1.

Table 1. Pts characteristics at diagnosis and types of treatments.

Age	<50	3 (9%)
	50<years<70	12 (36%)
	>70	18 (55%)
	Median	67 (range 38-81)
Gender	Male	22 (67%)
	Female	11 (33%)
Smoking habit	Active smokers	16 (48.5%)
	Former smokers	16 (48.5%)
	Never smoked	1 (3%)
Comorbidity	Cardiac	23 (70%)
	Pulmonary	7 (21%)
	Kidney	4 (12%)
	Autoimmune	3 (9%)
	Neurological	1 (3%)
	Others	20 (60%)
PS-ECOG	0	17 (52%)
	1	11 (33%)
	2	5 (15%)
M-stage at time of diagnosis	Brain	11 (33%)
	Lungs	26 (79%)
	Liver	15 (46%)
	Bone	14 (42%)
	Pleura	5 (15%)
	Adrenal glands	11 (33%)
	Lymph nodes	29 (88%)
Treatments after CT-IT	IT alone	24 (73%)
	TRT	7 (21%)
	PCI	3 (9%)
Thoracic RT (Total Dose)	39 Gy (3Gy/Fx)	4 (58%)
	45 Gy (3 Gy/Fx)	3 (42%)
PCI	25 Gy (2.5Gy/Fx)	3 (100%)

Results: Median follow up was 8 months (range: 20-1). All pts were treated with 4 cycles of first line platinum-based CT-IT (CBDCA, VP16 and Atezolizumab). Twenty-four pts also received maintenance IT with atezolizumab afterwards (median=7 cycles). Consolidative TRT was delivered to 7 respondent pts and prophylactic cranial irradiation (PCI) to 3 of them. Median and estimated 1-year OS was 7,8 months and 36.5%±SE8.8% respectively. Median and estimated 1-yr PFS was 5.3 months and 19.7%±SE8.0% respectively. At univariate analysis the use of consolidative TRT was a positive statistically significant prognostic factor in terms of OS (p< 0,02) as well as PS ECOG=0 (p<0,001) and no brain metastases (MTS) (p<0,02) at diagnosis. TRT also influenced OS (p<0,05) as well PS ECOG=0 (p<0,0001). Pts with brain MTS (p< 0,06) had a higher risk of death. G2 or more toxicities were reported in 20 patients (62,5%): neutropenia was the most common (17/20, with 3 patients experiencing life threatening toxicity) followed by anemia (6/20), thrombocytopenia and pulmonary toxicity (both 3/20), gastrointestinal and hepatic toxicity (both 2/20). No significant differences in terms of symptomatic side effects were found in patients who received also TRT or PCI.

Conclusions: In our study clinical outcomes, such as PFS and OS, seem to be comparable to registrative randomized clinical trials. In pts treated with TRT, safety was satisfactory and clinical outcomes were positively influenced. Larger cohorts of patients and longer follow-up are needed to further confirm these results in clinical practice.

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THE ASSOCIATION BETWEEN STEREOTACTIC EXTRA-CRANIAL RADIOTHERAPY AND THE USE OF TKI IN ONCOGENE ADDICTED NSCLC PATIENTS: A RETROSPECTIVE ANALYSIS FROM TWO CENTERS

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Aims: The use of Tyrosine Kinase Inhibitors (TKI) has revolutionized the survival of oncogene-addicted non-small cell lung cancer (NSCLC) patients. The addition of stereotactic radiotherapy (SRT) to drug-resistant metastasis allows to maintain the same therapy without switching to a new line and to extend the time to disseminate disease. The aim of this study is to analyze the safety of the association between TKI and extra-cranial SRT in NSCLC patients and to evaluate the timing of combination in real world clinical practice.

Method: We retrospectively collected data of oncogene-addicted NSCLC treated from two Italian centers from 2013 to 2022. Patient underwent a SRT on resistant extracranial metastases within 30 days from the administration of TKI. Acute toxicity was evaluated within 6 months from the end of the SRT using the Common Terminology Criteria for Adverse Events (CTCAE) v.5. Kaplan-Meyer curves were used to analyze the Progression Free Survival (PFS) and the Overall Survival (OS).

Results: We collected data from 17 patients, treatments and patients characteristics are summarized in Table 1. Median age at diagnosis was 68 years (ranging from 44 to 79 years). All patients have been diagnosed with adenocarcinoma, the majority (76%) of them presented the EGFR mutations. The SRT has been delivered mainly to lung sites (76%) using mostly volumetric modulated arc therapy (VMAT) technique (47%) in 5 fractions (52%). Only 3 patients had a Grade 2 toxicity:

one was a urinary tract infection, unrelated to treatments, two patients had experienced cough G2 related to SRT. Toxicity mean onset was 30 days after SRT (ranging from 7 to 56 days). After a mean follow up of 12 months the median OS was 15 months (CI 95%, 12-23 mo) and the median PFS was 9 months (CI 95%, 4-50 mo). Only 4 patients showed progressive disease in field (24%) with a median time to progression of 6 months. All patients have been instructed to suspend TKI during SBRT, 8 patients (47%) have been suspended TKI also before and after SRT for seven days or less.

Conclusions: Concomitant administration of TKI and extracranial SRT does not seem to increase any kind of toxicity, in our casistic we didn't experience interstitial pneumonia in patients undergoing SRT for lung metastasis. Our findings suggest that there is no necessity on TKI suspension before or after SRT; prospective analysis is required to confirm these data.

Table 1. Pts characteristics at diagnosis and types of treatments.

Patients characteristics	n° of patients/17 (percentage)
Sex	
- Female	- 14 (82%)
- Male	- 3 (18%)
Smoke habit	
- never smoker	- 8 (47%)
- ex smoker	- 7 (41%)
- unknown smoking habit	- 2 (12%)
Stage at diagnosis	
- II	- 1 (6%)
- III	- 6 (35%)
- IV	- 10 (59%)
Histology	
- Adenocarcinoma	- 17 (100%)
Mutation status	
- EGFR	- 13 (76%)
- Exon 19	- 9 (52%)
- Exon 21	- 3 (18%)
- Uncommon	- 1 (6%)
- ALK	- 3 (18%)
- KRAS	- 1 (6%)
Drugs	
- Afatinib	- 3 (18%)
- Gefitinib	- 4 (24%)
- Erlotinib	- 2 (12%)
- Osimertinib	- 5 (28%)
- Alectinib	- 1 (6%)
- Crizotinib	- 2 (12%)
Site of SBRT treatment	
- Lung	- 13 (76%)
- Nodal	- 3 (18%)
- Liver	- 2 (12%)
- Muscle	- 1 (6%)
Technique	
- IMRT step and shoot	- 6 (35%)
- VMAT	- 8 (47%)
- Tomotherapy	- 2 (12%)
- Cyber Knife	- 1 (6%)
No of Fraction	
- 3fx	- 3 (18%)
- 4fx	- 1 (6%)
- 5fx	- 9 (52%)
- 8fx	- 4 (24%)

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IMPACT OF IMAGE FILTERING AND ASSESSMENT OF VOLUME-CONFOUNDING EFFECTS ON CT RADIOMIC FEATURES AND DERIVED SURVIVAL MODELS IN NSCLC- BACK TO BASICS IN THE ERA OF RADIOMICS: AN EXPLORATIVE STUDY ON THE LUNG-1 DATASET

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Aims: No evidence supports the choice of specific imaging filtering methodologies in radiomics. As the volume of the primary tumor is a well-recognized prognosticator, our purpose is to assess how filtering may impact the feature/volume dependency in computed tomography (CT) images of non-small cell lung cancer (NSCLC), and if such impact translates into differences in the performance of survival modeling. The role of lesion volume in model performances was also considered and discussed.

Methods: Four-hundred seventeen computed tomography (CT) images NSCLC patients were retrieved from the NSCLC-Radiomics public repository. Pre-processing and features extraction were implemented using Pyradiomics v3.0.1. Features showing high correlation with volume across original and filtered images were excluded. Cox PH with LASSO regularization and CatBoost models were built with and without volume, and their concordance (C-) indices were compared using Wilcoxon signed-ranked test. The Mann Whitney U test was used to assess model performances after stratification into two groups based on low- and high-volume lesions.

Results: Radiomic models significantly outperformed models built on only clinical variables and volume. However, the exclusion/inclusion of volume did not generally alter the performances of radiomic models. Overall, performances were not substantially affected by the choice of either imaging filter (overall C-index 0.539-0.590 for Cox PH and 0.589-0.612 for CatBoost). The separation of patients with high-volume lesions resulted in significantly better performances in 2/10 and 7/10 cases for Cox PH and CatBoost models, respectively. Both low- and high-volume models performed significantly better with the inclusion of radiomic features ($p < 0.0001$, Figure 1), but the improvement was largest in the high-volume group (+10.2% against +8.7% improvement for CatBoost models and +10.0% against +5.4% in Cox PH models).

Conclusions: Radiomic features complement well-known prognostic factors such as volume, but their volu-

me-dependency is high and should be managed with vigilance. The informative content of radiomic features may be diminished in small lesion volumes, which could limit the applicability of radiomics in early-stage NSCLC, where tumors tend to be small. Our results also suggest an advantage of CatBoost models over the Cox PH models.

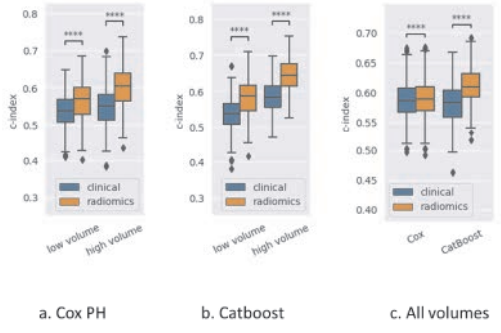

Figure 1. Performance of radiomic models (orange boxes) against clinical models (blue boxes) on two disjoint sets of patients stratified by low-volume and high-volume lesions. The left plot (a) shows the Cox PH model, and the center plot (b) shows the CatBoost model and the right plot (c) shows Cox PH and CatBoost performances when all volume lesions are included.

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FEASIBILITY AND SAFETY IN LUNG RE-IRRADIATION WITH STEREOTACTIC BODY RADIOTHERAPY (SBRT): OUR EXPERIENCE

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Aims: The data on the safety and feasibility of SBRT treatments have led to the increase of this technique in patients with early-stage inoperable primary lung cancer. The SBRT technique obtains excellent results in local disease control and improvement in overall survival. However, few studies are present on the use of SBRT in the reirradiation of relapses or second primary lung cancers. We have reviewed the outcomes of these patients treated at our radiation oncology department.

Methods: From May 2020 to February 2022, we re-treated 13 local recurrences or second lung tumors with the SBRT technique in 10 patients previously irradiated. All patients had histologically confirmed primary lung cancer. The characteristics of the patients and the treatments are shown in the table. Patients were excluded from a systemic therapy or surgical approach after multidisciplinary discussion.

Results: The median age of the patients at the time of re-treatment was 75 years. The median duration of follow-up was 15 months (range of 4-24 months). Local control was 92%. The most common fractionation used at the time of re-irradiation was 50 Gy into five fractions (range 25-60 Gy into 3-8 fractions). The median time from first radiotherapy treatment to reirradiation with SBRT was ten months. Acute toxicities of grades 1-2 were recorded in 30% of patients, but no grade 3 or higher. Chronic G3 toxicities were recorded in 2 patients with severe cardiovascular or respiratory comorbidities. All patients are currently alive. Three patients (30%) underwent new regional disease progression and further SBRT treatment after a new dosimetric study that allowed its feasibility. The follow-up of these patients is too short of giving us meaningful information even though none have experienced acute toxicities.

Conclusions: SBRT is a suitable treatment for regional recurrent or new primary lung tumors in patients previously treated with various thoracic radiotherapy regimens and that are not eligible for other local or systemic therapies. SBRT with a good toxicity profile and optimal local control is a valid salvage therapy in patients with few therapeutic options. However, the follow-up time and the limited number of patients treated require further confirmation.

Table 1.

Patient Characteristics	Median (Range)
Age (years)	75 (66-87)
Prior toracic RT dose (Gy)	50 (35-60)
Intervall between RT (mo)	10 (6-18)
Prior thoracic RT	CF 1 (10%) HF 2 (20%) SBRT 7 (70%)
Retreatment RT dose	50 (25-60)
Number of fractions	5 (3-8)
Recurrence/New primary lung tumor	Ipsilateral lung 7 Regional node recurrence 4 Controlateral lung 2
Acute toxicity G1-G2	3 (30%)
Acute toxicity ≥3	4 (30%)
Late toxicitiy G1-G2	5 (30%)
Late toxicity ≥3	6 (30%)

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CLINICAL OUTCOMES IN LOCALLY ADVANCED LUNG CANCER PATIENTS TREATED WITH SIMULTANEOUS CHEMORADIOTHERAPY FOLLOWED BY DURVALUMAB: A MONOCENTRIC DAILY CLINICAL PRACTICE

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Aims: To evaluate the feasibility and clinical results in daily clinical practice treating locally advanced non-small-cell-lung cancer (LA-NSCLC) patients in stage cIIIA-cIIIC using concomitant radiation therapy (RT) plus chemotherapy followed by Durvalumab according to PACIFIC trial.

Patients and Method: we evaluated clinical stage III NSCLC patients that received or ended curative RT (IMRT/VMAT) at 54-66 Gy in 27-30 Fx concomitantly to Carboplatin AUC2 + Paclitaxel 45 mg/mq weekly, and (for eligible patients) additional consolidation Durvalumab 10 mg/mq every 2 weeks for 12 months, in the second half of the 2021. All patients received a multidisciplinary recommendation for treatment.

Results: 14 patients with a median age of 70.5 yo, 7 female, 7 male are here described. The median dose was 60Gy. Every patient received one between DLCO, spirometry or scintigraphy pulmonary perfusion in order to evaluate respiratory function as some eligibility criteria for RT. During the elaboration of the treatment plan, several dose constraints have been granted (target lung: V20<28%, MeanDose < or = 13Gy, V5<40%. Contralateral lung: V5<20%, MeanDose <5Gy). Furthermore, supportive therapy has always been prescribed. During the follow-up, we evaluated clinical parameters such as G.I. symptoms (reflux, dysphagia), cough, dyspnoea and actinic pneumonia, during and at the end of the treatment. 5/14 patients received Durvalumab; only 1/5 patients had to stop immunotherapy infusion (2/26 infusions done) due to severe pulmonary toxicity, while 4/5 completed the consolidation immunotherapy without any complication. 0/14 treated patients presented actinic pneumonia. 7/14 patients presented moderate to severe cough, definitively solved after 6 months; 7/14 patients didn't present cough at all; 7/14 patients presented G.I. symptoms and in 3/7 esophageal reflux remained or got worse. 10/14 presented moderate dyspnoea, 6 of 10 solved the symptoms at the end, while 4 of 10 present slight dyspnoea nowadays, and 1 of 4 needs O2 sostitutive therapy. 2/14 patients presented fibrosis.

Conclusions: Basing on the results, we can assume that if the dose constraints are strictly respected and the supportive therapy is correctly assumed, the simultaneous chemoradiotherapy and durvalumab represents a valid and feasible therapeutic option for patients accurately selected in a multidisciplinary setting. This kind of treatment can be used in daily clinical practice.

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TOLERANCE AND OUTCOMES AFTER LUNG SBRT FOR PRIMARY EARLY STAGE LUNG CANCER: ANALYSIS OF ACUTE/LATE MORBIDITY, LOCAL CONTROL AND SURVIVAL IN A RETROSPECTIVE SERIES OF 27 PATIENTS TREATED AT A SINGLE ISTITUTION

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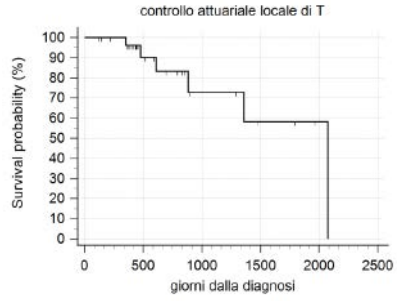
Aims: We retrospectively evaluated toxicities and outcomes of SBRT for primary T1-T2N0M0 early stage lung cancer in 27 consecutive patients (pts).

Method: Between September 2015 and December 2021, a single-institution cohort of 27 medically inoperable patients with early-stage lung cancer received lung SBRT. Median age was 77 years (range:58-89), Karnofsky performance status of 90(range:60-100). All pts were discussed in a multidisciplinary setting. 18F-FDG PET/CT and baseline respiratory function tests were performed before SBRT in all pts. A positive PET/CT scan and an increase in the size of the lesion at CT scan were mandatory for pts in which histology was not available (PET scan-directed SABR strategy: >85% probability of malignancy). Histological diagnosis was obtained in 83.9 % pts. In the remaining 26.1 % due to high risk of complication no biopsy was performed. In our series of 27 pts we performed 29 treatments for T1 (n=25) and T2 (n=4), central (n=4) and peripheral (n=25) primary lung tumours. Acute and late toxicity were scored according to CTCAE v4.3. The prescribed dose ranged from 48Gy to 60Gy in 3-8 fractions. Twenty-one pts (72%) received ablative doses of ≥100Gy BED10, range:100Gy-180Gy. We used 4DTC acquisition to identify the internal target volume;ITV-PTV margins: 5mm anisotropic.Treatment plans were studied on Varian Eclipse TPS and delivered by RapidArc® with IGRT technique.

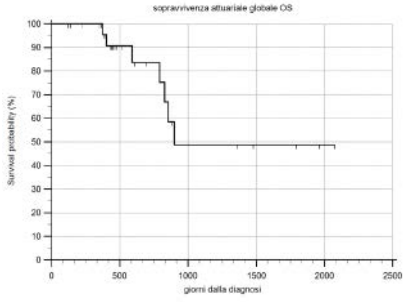
Results: Early side effects occurring within 6 weeks of treatment were uncommon: only 1 case of G1 acute pulmonary reaction (4%) was recorded. Late toxicity, at 6 months from SBRT, was as follows: pulmonary G1 reactions in 15 pts (56%), pulmonary G2 in 1 pt (4%), chest wall G1 in 1 pt (4%). No Grade 3–4 acute and late reactions were recorded. Median follow-up was 18 months (range: 2-75 months) and median survival for all 27 pts

was 30 months. According to Kaplan-Meier analysis: actuarial 2- and 3-yr LC of irradiated lesions (n=29) was 83.2% (IC95%:65,2%-100%) and 72.8% (IC95%:48,1%-92.3%), respectively; 2- and 3-yr OS for the whole series of pts (n=27) was 83,7% (IC95%:66,4%-100%) and 48,8% (IC95%:20,4%-77,2%), respectively; 2- and 3-yr CSS was 92,3% (IC95%:77,8%-100%) and 61,5% (IC95%:30,8%-93,5%), respectively (Figure 1a-b-c).

Conclusions: Our single institution data confirm SBRT as a safe, well tolerated and effective treatment option for early stage lung cancer, with excellent results both in terms of disease local control and survival rates.



A.



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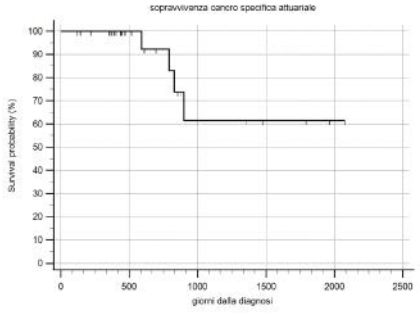

C.

1. Figura 1. A - Local Control; B – OS; C - CSS

Figura 1. A - Local Control; B – OS; C - CSS.

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C-PAP & SBRT IN CENTRAL AND ULTRA-CENTRAL LUNG CANCER: A CASE REPORT

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We describe a clinical case, treated by a combined approach of SBRT & C-PAP as breath-holder, to evaluate efficacy, safety and manageability: a 73 years old patient with a squamous cell lung cancer, stage cT3 N0. PET-CT showed a centroparenchymal tumor (30 x 30 x 50 mm) in the left superior lobe touching the aortic arc, SUV 16.98.

C-PAP has long been safely used in patients with respiratory failure and chronic obstructive pulmonary disease to maintain airway patency. It provides a constant stream of pressurized air to the upper airways and lungs. The physiologic effects expected during C-PAP are hyperinflation of the lungs, stabilization and diaphragm flattening. We made frameless simulation, in supine position and Combifix immobilization, with slow CT in axial mode, 2.5 mm thickness, 4.0 sec. time gantry rotation. We applied C-PAP under 10 cm H2O for 5 minutes, with a pO2 30%. Contouring phase was performed using Monaco TPS with Montecarlo alghorytm. We identified the lesion as CTV with no expansion for the PTV (0 mm). The OAR were left and right lungs, heart, oesophagus and spinal cord. The dose was specified to 95% of the PTV. All the dose constraints were respected. We prescribed SBRT with a dose of 750 cGy/fr x 8 fr (total dose 6000 cGy). In November '19, the patient started the treatment with VMAT and 6 MV FFF photons, to speed up the procedure. The set up was checked by daily cone beam TC. In September '20 a PET-TC showed that lesion's diameter was 2 mm (SUV 2,38) but there was a new paraortic lesion (diameter 15 mm, length 4 cm, SUV 7,5) invading the left wall of aorta. Due to the position, it wasn't possible to biopsy it. We planned a second treatment with SBRT tecnique. TC simulation was performed with the same setting, except for the use of the C-PAP system, because of the risk of aerosolization due to COVID-19. Because of the tumor 's site and the proximity of the descendent aorta, we prescribed was 400 cGy/fr x 15 fr (total dose 6000 cGy). After 1 year, the patient is in good clinical conditions. PET-TC showed a mild FDG uptake (3,2) for the second lesion, geometrically and precisely referred to the 95% isodose volume. Combination of C-PAP & SBRT provides a very effective treatment and a safe approach in the management of a lung tumor. At the end of the pandemic era we wish to resume this system and recuit a larger number of patient to optimize customized treatment associating this simple, safe and not expensive technique with lung SBRT.

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PREVENTION OF LATENT TUBERCOLOSIS REACTIVATION DURING CONCOMITANT RADIO-CHEMOTHERAPY IN LUNG ADENOCARCINOMA: A CASE REPORT

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Aim: Lung cancer is one of the greatest common cancers. Recent evidences have shown the inflammatory process as risk factor of cancer. Chronic inflammation and fibrosis due to tubercolosis (TB) can induce genetic mutation and alterations which may increase the risk of lung cancer. On the contrary many cases where antineoplastic therapies reactivated latent Mycobacterium tuberculosis are described in literature.

Matherials and Methods: Here we present a case of a 66 year old man, smoker, suffering of emophtoe and thoracic pain. Chest X-ray revealed air space consolidation in the right superior lobe and chest Computed Tomography (CT) showed an 57mm opacity in the right superior lobe, with lymphadenopathies in 10th and 11thc right levels and calcific lymphnode in 7th level. No evidence of pleural effusion. CT driven biopsy was positive for lung adenocarcinoma with KRAS mutation. The physical examination was unremarkable. His medical hystory was positive for tubercolosys in childood, but no clinical records were available. He completed clinical staging with brain Magnetic Risonance (MR) and Positron Emission Tomography (PET) CT, that were negative for metastatic spread. We discussed the case with multidisciplinar team (MDT) whith pulmonologist, oncologist, thoracyc surgeon and radiologist and the patient (pt) was staged as cT3N1M0, IIIA sec VIII TNM edition.

Results: Surgery was refused by the pt, so he was switched to concomitant radio-chemotherapy but there was the remote chance of reactivation of a latent mycobacterium during cancer treatment. So in MDT we decided for a first line prevention antiTB therapy prescribed by pulmonologist, started at the time of radiochemotherapy and lasted for 6 months. Patients received daily radiotherapy up to 60Gy in 30 fractions, combined with doublet platin based chemotherapy, with Nicozid 300mg/die + B6 Vitamine with optimal oncological response and no signs of TB reactivation.

Conclusion: The combination chemo and radiation therapy elevates the risk of reactivation of chronic and indolent infections so when data about eradicant therapy aren't available, the prevention of latent TB is a safe and well tolerated option that can prevent life threatening evolutions.

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MANAGEMENT OF A MODERATE PULMONARY TOXICITY IN A PATIENT RECEIVING DURVALUMAB

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Aims: We report the case of a bilateral immune-related pneumonia in a Stage IIIA Non Small Cell Lung Cancer elderly patient after the first administration of Durvalumab subsequent to a primary RTCT.

Materials and Methods: B.L.S.76-year-old female patient, has been diagnosed with a locally advanced NSCLC (PDL-1 expression: 70%) of the left lower lung. The patient was eligible for concurrent RTCT followed by consolidation therapy with Durvalumab in case of no progression, so she underwent VMAT therapy (66 Gy at 2 Gy per once-daily fraction) and, in addition, concomitant chemotherapy with 6 cycles of cisplatin 40 mg/mq and taxolo 30 mg/mq once a week, with good tolerability and low toxicity. A total body CT performed 4 weeks after the end of the treatment to assess the clinical response, revealed a partial response. According to PACIFIC trial the patient started Durvalumab as consolidation therapy. 3 days after the 1st administration the patient went to the emergency room manifesting dyspnea G4, productive cough. She was tested positive for Coronavirus. The CT scan was negative, so she was discharged with antipyretic therapy. 2 weeks later, as she clinically recovered and tested negative for Covid, she received the 2nd dose of Durvalumab. After three weeks, when the patient should have received the 3rd infusion, she complained of a worsening of the respiratory symptoms. Physical examination showed presence of exhalation wheezing. Durvalumab infusion was canceled and a CT-scan was performed showing a flogistic process of uncertain origin. Therapy with Methylprednisolone 1mg/kg was initiated in suspicion of immuno-releated pneumonia. After one month, respiratory symptoms improved and a new CT showed a reduction in the flogistic areas with stable disease. Considering the clinical and radiological resolution, we resumed therapy with Durvalumab. The patient has now completed 6 doses of therapy, she is in excellent overall condition and the last CT revaluation showed stable disease.

Results: Corticosteroid therapy solved our patient's G2 pneumonia, most likely immuno or radiation related, allowing her to quickly resume durvalumab in order to increase the chances of oncological control.

Conclusion: This case shows the importance of an early diagnosis of immuno-related pneumonia and of an immediate start of a steroid therapy. In case of a moderate toxicity it is safe to resume immuno-therapy, in order to increase the chances of oncological control of the disease.

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PREDICTORS OF LOCAL CONTROL AND SURVIVAL FOR STEREOTACTIC FRACTIONATED RADIOTHERAPY (SFRT) IN PATIENTS WITH BREAST CANCER BRAIN METASTASES

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Aims: To assess potential predictive-prognostic factors for local control (LC) and overall survival (OS) in patients with breast cancer brain metastases (BCBM) treated with Stereotactic Fractionated Radiotherapy (SFRT)

Method: Patients with BCBM treated at our Institution from 2019 to 2021 with SFRT were retrospectively evaluated. Patients were gathered in 4 groups based on histotype [Luminal A (LumA), Luminal B (LumB), Her-2+ and Triple Negative (TN)]. For each patient Diagnosis Specific Graded Prognostic Assessment (DS-GPA) based on age, Performance Status (PS), number of brain metastases (nL), extracranial disease (ED) and brain lesions date of diagnosis was calculated. Monoclonal antibody therapy (MAT), grading, lesion site and total PTV volume (PTVt) were included in the analysis as a potential predictor of oncological outcomes. Association between LC and categorical predictors was calculated with Chi Squared test, while the association between LC and continuous predictors (PS, DS-GPA, nL, PTVt) with Mann-Whitney test. OS was calculated from date of SFRT until death or last follow-up; continuous predictors were transformed into categorical variables using the Youden Index method. Patients were stratified into high/low risk groups according to categorical predictors and Kaplan Meier curves were compared between the groups using log rank (LR) test. The prognostic value of each feature was assessed using the concordance index (CI) of univariable Cox regression.

Results: Seventeen patients accounting for 61 brain lesions were evaluated. Patients were treated with SFRT using a mono-isocenter technique (HyperArc) and the prescribed dose was 24-27 Gy in 3 fractions. Exploratory analysis showed that LC is linked to histotype and MAT in Her-2 + patients. LC is 66.7% in LumB, 40% in LumA, 33.3% in Her-2+, while TN group was not responder. 62.5% of patients who underwent MAT had greater LC (P=0.092). Patients with high rate of ED (58.3%) had better LC (P=0.026) and more favorable histotype at diagnosis (P=0.003). Promising prognostic features were PTVt (CI=0.75, LR p-value=0.08), nL (CI=0.74, LR p-value=0.08), DS-GPA score (CI=0.71, LR p-value=0.07) and histotype (CI=0.85, LR p-value=0.02). Median OS was 13.5 months for LumB, 9 months for LumA, 4 months for Her-2+ and 2 months for TN respectively.

Conclusions: This preliminary study showed that histotype, MAT, ED, nL and DS-GPA score were related to LC and OS in patients with BCBM treated with SFRT.

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ADVANCED VISION RT IMPROVES ACCURACY OF BREATH HOLD TREATMENT DELIVERY IN BREAST CANCER PATIENTS

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Aims: Adjuvant Radiotherapy (RT) represents the standard of care for breast cancer patients; albeit, it can be associated with long-term secondary adverse effects, principally concerning heart and lung toxicity. Deep Inspiration Breath Hold (DIBH) technique is an optimal strategy to minimize dose to cardiac structure. A technique for monitoring patient position during DIBH is Surface Guided Radiation Therapy (SGRT). We aimed to estimate setup accuracy with the use of Vision AlignRT (VA) (Vision RT Ltd.), comparing the standard version with the advanced version, Vision Advanced AlignRT (VAD), in a large cohort of patients undergoing DIBH RT treatment of left breast cancer.

Methods: Patients affected by left breast cancer receiving adjuvant DIBH RT were evaluated. Patients positioning was performed by SGRT. The cohort of patients was divided in 4 groups based on treatment volume and version of Vision employed: left breast only, positioned with VA (G1) and VAD (G2); left breast and supraclavicular lymph node chain and/or Internal mammary chain (CMI), positioned with VA (G3) and VAD (G4). Accuracy of positioning was evaluated by means of CBCT. Differences between groups were assessed by two tailed t-test. Data were deamed as statistically significant if $P<0.001$.

Results: 154 patients treated with DIBH RT were evaluated by CBCT (total number=1440), either for left breast only patients (patients 123, 879 CBCT) and/or left breast supraclavicular lymph node chain and/or CMI (patients 21, 561 CBCT). The interfractional displacement on the longitudinal, lateral, and vertical directions for G1 versus G2 was reduced when the advanced version was used: 0.264±0.001 versus 0.214±0.001 centimeters (cm); 0.194±0.001cm versus 0.180±0.001cm; 0.252±0.001cm versus 0.213 ±0.001cm, respectively, with significant difference ($P<0.001$) in all directions except for lateral. The interfractional displacement on the longitudinal, lateral, and vertical directions for G3 versus G4 was also reduced when the advanced version was

used: 0.264±0.001cm versus 0.214±0.001cm; 0.194±0.001cm versus 0.180±0.001 cm; 0.252±0.001 versus 0.213 ±0.001 cm, respectively, all with significant difference (P <0.001).

Conclusions: Positioning with VAD is more accurate then positioning with the VA, in both patients treated for left breast only radiotherapy and for breast and supraclavicular lymph node chain or/and Internal mammary chain. Greater advantage is showed in patients treated to breast and lymphnodes.

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FAST AND FAST FW PROTOCOLS: ACUTE SKIN TOXICITY, DOSIMETRIC RESULTS, AND PATIENTS' ANTHROPOMETRIC PARAMETERS

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Aims: Recent trials (FAST and FAST FW) have reported quality results to support ultrahypofractionated whole breast irradiation (ultra-HF-WBI) for early stage invasive breast cancer (ESBC). We discuss factors influencing the implementation of this schedule at our Institution.

Methods: ESBC patients were treated with 28.5 Gy in 5 fractions once a week (FAST protocol), or 26 Gy over 1 week (FAST FW), using the 3D-CRT field-in-field (FIF) technique at a single Institution. Clinical target volumes (CTVs), dosimetric parameters, and tumour characteristics were recorded and analysed. The parameters measured to assess the breast size were the cup size, the nipple-to-pectoral muscle distance (NPD), and the maximum medio-lateral thickness (MLT) along tangential fields. Adverse skin reactions were assessed according to CTCAE v. 5.0 at the end of treatment. Clinical follow up was performed at 1 month, 3 months, and 6 months.

Results: Between December 2020 and May 2022, a total of 76 patients, median age 69 [range 51-85], with ESBC were treated with adjuvant radiotherapy; 39 of them with the FAST schedule and 37 of them with FAST FW scheme. 65% of patients had fair skin (skin phototype I/II according to the Fitzpatrick scale). The median CTV volume was 375.76 cm^3 [60.29-1011.18] with a median NPD of 4.7 cm [1.7-9.0] and a median MLT of 21.8 cm [14.3-32.3]. The 5.3%, 32.9%, 39.5%, 18.4%, 1.3% and 2.6% of patients wore an A, B, C, D, E and F bra cup-size, respectively. CTVs registered a median V 95% of 99.6% [95.4-100.0] and a median V105% of 0.1% [0.0-4.7]. The median 105% isodose was 0.9 cm^3 [0.0-48.0] of whom 0.1 cm^3 [0.0-5.2] in the first centimeter below the skin surface. Lung and heart dose constraints were never exceeded. The registered toxicities were a case of edema at 1 month and a case of mastitis at 6 months. Anti-inflammatory drugs and anti-edema were prescribed.

Conclusions: Our results confirmed the safety of the FAST and FAST FW protocols in terms of acute post-RT-related skin toxicity; offering ultrahypofractionation reduces the number of hospital visits and it is cost-effective.

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ONE WEEK WHOLE BREAST ADJUVANT RADIOTHERAPY WITH SURFACE-GUIDED SYSTEM IN ELDERLY/FRAIL PATIENTS AFTER BREAST CONSERVING SURGERY: SINGLE EXPERIENCE DURING COVID-19 PANDEMIC OUTBREAK

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Aims: One week radiotherapy (RT) in breast cancer (BC) patients (pts) is a current treatment option based on the FAST-FORWARD trial results and since the onset of Covid-19 pandemic outbreak. The purpose of this retrospective report is to evaluate the tolerance, in terms of acute toxicity rate of elderly/frail BC pts treated with adjuvant ultra-hypofractionated RT using a surface-guided (SG) system set-up in the past two years.

Method: From June 2020 to June 2022, BC pts receiving 26 Gy in five consecutive fractions (5.2 Gy/fr) to the whole breast after breast-conserving surgery (BCS) were assessed. Inclusion criteria were: pT1/pT2 invasive BC, no or limited axillary involvement (pN0/pN1), age ≥ 70 years or frail women with disabling diseases. Target volumes and organ at risk were defined and plan were evaluated according to the FAST-Forward trial planning objectives. Patient set-up was performed via AlignRT®, a non-invasive 3D imaging system tracking patient's position before and during RT. A daily cone beam computed tomography scan was daily verified by a radiation oncologist to correct residual set-up errors. Early and late toxicities data were recorded using the Common Terminology Criteria for Adverse Events version 5.0.

Results: A total of 61 patients completed the whole treatment with no interruptions and were evaluated. Median age was 75 (range: 66-90) years. Most of pts were T1 (87%), while the remaining were T2 (13%). 74% of the pts were axillary status negative, only 26% were pN1. None except 1 patient received chemotherapy. Patient characteristics are summarized in Table 1. With 8 months of median follow-up (range: 1-21 months) no acute G3 or higher skin toxicity were observed. Skin toxi-

city were collected at last RT fraction (G0: 49%, G1: 31%, G2: 20%), after 1-3 months (54 pts, G0: 37%, G1: 67%), 6 months post-RT (39 pts, G0: 49%, G1:51%) and 1 year later (26 pts, G0: 69%, G1: 31%).

Conclusions: Our preliminary report show that one-week whole breast RT after BCS seems feasible and safe with low acute toxicity rates in selected patients. The surface-guided RT system could be a useful tool both in optimizing set-up accuracy and improving tolerance to an ultra-hypofractionated RT schedule. Longer follow-up is needed to confirm these results also in terms of late toxicity and local control.

Table 1. Patient characteristics.

	Age		Side		Surgery type		Histology		Grading			pT		pN		ER status		HER 2 status	
	>70	< 70	R	L	BCS + SLN	BCS + ALND	BCS	IDC	INDC	G1	G2	G3	1	2	0	1	+	-	+	-
N (%)	56 (92)	5 (8)	31 (51)	30 (49)	51 (84)	8 (13)	2 (3)	39 (64)	22 (36)	12 (20)	39 (64)	10 (16)	53 (87)	8 (13)	45 (74)	16 (26)	59 (97)	2 (3)	1 (2)	60 (98)

Legend: SLN: sentinel lymph node; BCS: breast conserving surgery; IDC: invasive ductal carcinoma; INDC: invasive non-ductal carcinoma; L: left; N: number of patients; R: right.

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EVALUATION OF REPRODUCIBILITY AND TOLERANCE OF ACCELERATED PARTIAL BREAST IRRADIATION (APBI) WITH VOLUMETRIC MODULATED ARC THERAPY (VMAT) AND DAILY IMAGE-GUIDED RADIOTHERAPY (IGRT) IN A SELECTED SUBGROUP OF PATIENTS

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Aims: Accelerated partial breast irradiation (APBI) represents a valid alternative treatment for selected patients (pts) with early breast cancer (EBC). Aim of our study is to evaluate the reproducibility and tolerance of APBI with volumetric modulated Arc therapy (VMAT) and daily image-guided radiotherapy (IGRT) in a selected subgroup of pts.

Method: From March 2021 to April 2022 we enrolled 51 EBC pts aged > 60 years underwent lumpectomy and sentinel lymph node (SLN) biopsy, with placement of clips on the tumor bed. Prevalent histology was ductal, molecular subtype Luminal A, T stage T1-T2, tumor grade G1-G2 with negative margins and SLN. Two mm slices-Computed Tomography scan was acquired. The clinical target volume was drawn with isotropic 1.5 cm margin around the clips, to include radiological abnormalities and limited to 3 mm from skin. Isotropic 0.5 cm margin was added to obtain the planning target volume. Ipsilateral and contralateral lung, heart, left coronary artery (LAD) and contralateral breast were contoured as organs at risk. A total dose of 26 Gy in 5 once-daily fractions was prescribed. These constraints were adopted for VMAT optimization: PTV coverage V95% = 95%; maximal dose (Dmax) to PTV < 107%, ipsilateral lung V10 < 20%, contralateral lung V5 < 10%, heart V3 < 10%, LAD mean dose (Dmean) ≤ 5 Gy, contralateral breast Dmax < 1 Gy and Dmean ≤ 3 Gy. Daily cone beam CT (CBCT) was performed for pts set-up. Varian intrafraction motion review ability to automatically detect fiducial markers (FM) was used with kV images triggered every 60 degrees of gantry rotation during treatment. FM displacement from expected position was used for evaluating the reliability of CBCT pts positioning. Toxicities were evaluated using Common Terminology Criteria of Adverse Events scale at the end of RT, at 1 month and at 6 months after RT.

Results: All dose constraints were widely respected with PTV coverage V97% = 97%. The median of FM displacement was greater for the cross-plane axis, which was affected by respiratory movement, but remained ≤ 3 mm. RT was well tolerated. None of the pts reported any side effects during RT; during follow-up 5 pts experienced Grade 1 breast pain, 4 pts Grade 1 skin induration and hyperpigmentation.

Conclusions: APBI with VMAT technique was well tolerated with a very low toxicity profile. Intrafraction marker detection showed no significant bias with CBCT imaging and may prevent off-target irradiation when Auto Beam hold is activated.

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ULTRAHYPOFRACTIONATED (UHF) RADIOTHERAPY IN BREAST CANCER: UPDATE TO 24 MONTHS

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Aim: to reduce treatment time in patients (pt) with early stage breast cancer (EBC) undergoing breast conserving surgery (BCS) during the COVID-19 pandemic, as suggested by the radiotherapist oncology community.

Methods: From June 2020 to June 2022, we recruited 50 women ≥60 years old, with EBC, undergoing BCS (pT1-2(<3 cm) pN0), G1-2 and negative margins. The prescribed dose was 28.5 Gy in once weekly fractions over 5 weeks. The primary end-point was local tumor control, acute and chronic toxicity (tox) end esthetic outcomes. Secondary end points were impact on quality of life (QoL) and on waiting list. After a CT-scan, a whole breast irradiation 3D-planning was performed using opposite tangent with fields in fields, with 6 Mv photons, and subfields

to improve dose homogeneity. Skin tox was assessed with the RTOG score. In order to evaluate esthetic outcomes, two photos were taken for each pt (antero-lateral and antero-medial), at the beginning, at the end of the treatment, and then at 3, 6, 12, 24 months (mo) follow up.

Results: We enrolled 50 pt with mean age of 74 years (range 61-84). The median follow-up was 11 mo (range 0-24). The most common tox were acute erythema and edema and late breast fibrosis and shrinkage. With the limit of the short follow-up, no one developed recurrence and only one had significant esthetic changes with moderate fibrosis and breast shrinkage a 12 e 24 mo. Acute tox evaluated was not greater than G2, with 44 (88%), 45 (93.75%) pt respectively G0-1 at end radiotherapy and 3 mo later. Similarly, chronic tox evaluated was not greater than G2 with 40 (93.02%), 29 (90.62%) and 4 (80%) pt respectively G0-1 at 6, 12 and 24 mo. All patients showed a high level of satisfaction and among all patients who experienced tox, this impacted QoL only in 2 (8.6%) cases and with low entity. The UHF regimen reduces treatment sessions by 66.6% compared to the standard hypofractionated, with an obvious impact on waiting time list and on the risks of spreading COVID-19.

Conclusions: Once weekly UHF radiotherapy is a feasible alternative in the adjuvant management of EBC. It is well tolerated and particularly appreciated by pt, has a low acute and chronic tox and good cosmetic outcomes. Finally, it significantly reduces the risks of spreading COVID-19 and waiting lists.

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VMAT RADIOTHERAPY EXTENDED TO NODAL AREAS CONCURRENT TO ADJUVANT T-DM1 IN BREAST CANCER: WHICH TOXICITY TO WARRY ABOUT?

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Aims: Adjuvant Trastuzumab-emtansine (T-DM1) has been approved in the adjuvant treatment of non metastatic HER2-positive breast cancer (BC) patients with residual disease after neoadjuvant systemic therapy for 14 cycles. Usually few cycles coincide with the adjuvant radiotherapy (RT) delivery. Pulmonary and cardiac toxicity could be a big concern in case of concomitant RT on extend volumes including nodal areas treated in VMAT modality. Aim of this report is to evaluate the safety of this concurrent combination in terms of acute pulmonary and cardiac side effects.

Methods: 15 BC patients treated with T-DM1 concurrent adjuvant RT were treated between March 2020 and March 2022. Adjuvant T-DM1 was supplied at 3.6 mg/kg every 3 weeks. At least 1 cycle was concurrent with RT after 1-2 cycle before RT followed by more cycles. Adjuvant RT was delivered on chest wall with supraclavicular and CMI nodes in 7 patients; 3 patients were treated on residual breast and supraclavicular nodes; 2 patients on chest wall, CMI and axilla. VMAT-RT with 50Gy total dose in standard fractionation was delivered to all of them. A 10Gy boost was added in 5 patients. Left ventricular ejection fraction was assessed at baseline, before and 3 months after RT. Chest CT scan was prescribed 1 and 3 months after the end of RT. All toxicities were evaluated using Common Terminology Criteria of Adverse Events (CTCAE) version 4.0. Very strict dose constraints to OAR's like ipsilateral, controlateral lung and heart were observed. For ipsilateral lung a mean V5Gy < 55%, V10Gy < 45%, V20Gy < 25%, MLD < 12Gy were accounted; for heart a D mean < 5 Gy, V5 Gy < 50 %V30 Gy < 8% were obtained. In left sided BC (5 patients), a breath hold control system was useful to obtain lower goals.

Results: All observed patients completed the entire course of scheduled RT without interruptions. T-DM1 was shifted of one week due to G2 neutropenia in 1 patient. The number of T-DM1 cycles were delivered as scheduled. No cardiac or pulmonary events were recorded, neither late reactions were found at 1-3 months of follow up.

Conclusions: Although literature data report cardiac side effects and radiation pneumonitis in T-DM1 concurrent adjuvant RT and few data are available, in case of extended volumes treated with VMAT and T-DM1 in adjuvant setting, this combination seems to be safe.

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INTRAOPERATIVE RADIOTHERAPY (IORT) IN EARLY STAGE BREAST CANCER: A RETROSPECTIVE ANALYSIS OF A SINGLE CENTRE

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Aims: Breast cancer (BC) is the most frequently diagnosed in women. Whole breast irradiation following breast-conserving surgery is nowadays the standard treatment for early stage BC. Partial breast irradiation (PBI) reduces the treatment field in selected patients with low risk of recurrence. It delivers radiation dose only to the tumor bed and its periphery, which represent the most common sites for local recurrence (LR). PBI can be performed through different techniques, with encouraging results in literature: intraoperative radiotherapy (IORT), brachytherapy or external beam radiotherapy. We performed a retrospective analysis of patients who underwent breast-conserving surgery and IORT for early stage BC from 2011 to 2020 in our center.

Methods: In all patients IORT was performed soon after the surgical procedure with 50 kV X-rays through an Intrabeam device. Need for further treatments could then be discussed and a whole breast radiotherapy (WBRT) in addition to IORT could be programmed. For each patient we registered personal data, timing of diagnosis of BC, histological features, types and timing of treatments, date and site of recurrence of the disease, distant metastases, last follow-up, date of death, cause of death.

Results: Patients in study were 334, all female, with median age 72.1 years (45.0 - 88.8). Most of them were diagnosed with invasive carcinoma of no-special type (91.3%), grading G1-G2 (82.6%), less than 2 cm (90.1%), often with negative margins (76.6%), positive estrogen and progesterone receptors (98.5% and 92.2% respectively). In 76.9% there was no evidence of nodal involvement and in 79.9% no evidence of lymphovascular invasion. After histological findings were available 21% needed additional WBRT. After a median follow-up of 57 months (range 13-107 months), we found 14 cases of recurrence of disease (4.2%). Five patients developed nodal metastases (1.5%) and two distant metastases (0.6%). Four cases of recurrences appeared after IORT and WBRT. Fourteen patients (4.2%) died and the cause of death was BC in 3 of them.

Conclusions: Patients experienced an overall good outcome in terms of disease control, probably thanks to initial adequate selection and multidisciplinary management. The role of IORT as sole radiotherapy is still an object of study and almost a challenge: this analysis confirms how it allows to reach favourable results but at the same time not excluding further treatment.

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FIVE FRACTIONS ACCELERATED PARTIAL BREAST REIRRADIATION AFTER SECOND CONSERVATIVE SURGERY IN LOCALLY RELAPSED BREAST CANCER PATIENTS

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Aims: NRG Oncology/RTOG 1014 Phase 2 clinical trial concluded that for patients with recurrent ipsilateral breast cancer a second lumpectomy with a partial breast reirradiation to a total dose of 45 Gy delivered in 15 days with 1.5 Gy twice daily is feasible, achieving a second breast conservation in 90% of patients. Here we report the results of five fraction accelerated partial breast reirradiation performed in our department during the Covid19 pandemic.

Methods and Materials: Thirteen patients presenting an ipsilateral relapse after an intial pTis-pT2N3a breast cancer treated with conservative surgery and adjuvant radiotherapy to a median total dose of 50 Gy (37.5-50) +/- a boost of 10 Gy/5 fractions (4 patients) or 1 fraction of 12 Gy (electrons, one patient), were reirradiated from 03/2019-05/2022, after a second conservative surgery. Median age at reirradiation was 68 (50-77.7) years. Eight patients were left sided and 5 patients right sided. Three were lobular invasive tumors, the others ductal invasive. One was triple negative, one hormonal receptor positive-Her2 positive, 6 Luminal B Her2 negative and 5 Luminal A tumors. Median dimension of the relapse was 1.2 (0.18-2) cm. A 10 mm margin was added to the tumoral bed to obtain the clinical target volume (CTV), and 5 mm to CTV to obtain the planning target volume (PTV). A median dose of 26 (26-30) Gy in 5 fractions was prescribed to PTV.

Results: Median follow up was 14 (0-35.1) months. One patient was treated with VMAT (RapidArc, Varian, Palo Alto, CA), five with tomo-direct and 7 with tomo-helical technique (TomoTherapy, Accuray, Madison, WI). All patients are alive and none presented a local relapse. Only one patient presented an axillary lymph-nodal relapse. Two-year distant metastasis-free survival= 92.3% (see Figure 1). Acute and late toxicities were registered with CTCAE v5.0. Only 2/13 patients presented acute G1 erythema. Two of 12 evaluable patients presented late G1 edema (16.7%), 4/12 late G2 fibrosis (33.3%), and 1 G1 fibrosis (6.9%). Two other patients (16.9%) presented fat necrosis. No G3 acute or late events were registered.

Conclusion: In our Covid19 pandemic-driven experience, accelerated-partial breast re-irradiation is feasible, with excellent short-term local control and acceptable toxicity. Longer follow-up is needed to confirm these results.

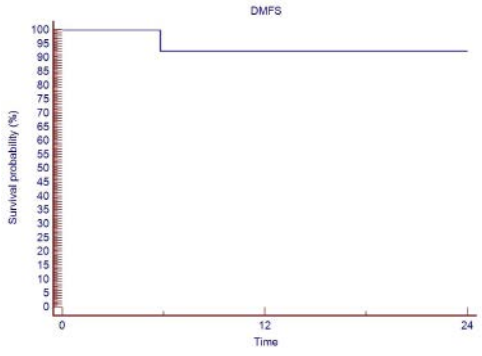

Figure 1. Two-year Kaplan Meier estimates of distant metastasis-free survival.

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ULTRA-HYPOFRACTIONATION FOR WHOLE BREAST RADIATION THERAPY IN EARLY BREAST CANCER PATIENTS

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Aims: To report on the early clinical outcomes of a prospective series of early breast cancer (EBC) patients treated with ultra-hypofractionated post-operative whole breast irradiation (WBI) after breast conserving surgery (BCS) and axillary management.

Methods: A prospective cohort of EBC patients was enrolled between May 2021 and May 2022. After BCS, all patients underwent WBI. Treatment schedule consisted of either 26 Gy in 5 fractions over one week (standard approach) or 28.5 Gy in 5 fractions over 5 weeks (reserved to elders). Patients were treated with inverse planned intensity modulated radiation therapy (IMRT) delivered with a static technique. Primary endpoints were patient's compliance and acute toxicity. Secondary endpoints included late toxicity, cosmesis, and ipsilateral breast tumour recurrence (IBTR). Acute toxicity was evaluated at the end of WBI and 3 weeks thereafter, according to the Common Terminology Criteria for Adverse Events (v. 6.0).

Results: A total of 54 patients was treated. 44 were treated with 26Gy/5fr/1w and 10 with 28.5Gy/5fr/5ws. Median age was 69. Most of the patients had right-sided tumors (55.6%), Q1 or Q1-Q2 localization (51.8%), pT1b or pT1c disease (61%), pN0 (68.5%), ductal histology (72.2%), Grade 2 (63%), Luminal A or B intrinsic subtyping (90.7%). Most of the patients underwent BCS and sentinel lymph node biopsy (74.1%) and adjuvant endocrine therapy (77.8%). See Table 1 for details. All patients completed the treatment program as planned. Maximum detected acute skin toxicity was: grade 1-2 skin hyperpigmentation (22.2%; 12/54); grade 1-2 erythema (18.5%; 10/54 pts); grade 1-2 pruritus (12.9%; 7/54 pts); grade 1 induration (12.9%; 7/54 pts); skin atrophy (9.2%; 5/54 pts); grade 1 oedema (0.55%; 3/54). No early IBTR was observed.

Conclusions: Ultra-hypofractionated WBI provides favorable compliance and early clinical outcomes in EBC after BCS.

Table 1. Patient and treatment characteristics.

Patient characteristics	N° (%)
Age	
Median (years)	69
Range (years)	47-88
Laterality	
Left-sided	24 (44.4)
Right-sided	30 (55.6)
Quadrant	
Q1	22 (40.7)
Q2	3 (5.5)
Q3	5 (9.3)
Q4	2 (3.7)
Q5	5 (9.3)
Q6	4 (7.4)
Q1-Q2	6 (11.1)
Q1-Q3	3 (5.5)
Q3-Q4	3 (5.5)
Tumor characteristics	**N (%)**
Pathological tumour stage	
pTis	3 (5.5)
pT0	3 (5.5)
pT1mic	1 (1.6)
pT1a	4 (7.4)
pT1b	13 (24)
pT1c	20 (37)
pT2	10 (19)
pT3	0 (0)
Pathological nodal stage	
pN0	37 (68.5)
pN1mic	2 (3.7)
pN1a	3 (5.5)
pN1b	0 (0)
pN1c	0 (0)
pN2	0 (0)
pNx	12 (22,3)
Histology	
Ductal	39 (72.2)
Lobular	4 (7.4)
Mixed ductal/lobular	1 (1.6)
Mucinous carcinoma	4 (7.4)
Papillar carcinoma	3 (5.5)
Foci of intraductal carcinoma	2 (3.7)
Paget	1 (1.6)
Grading	
G1	7 (13)
G2	34 (63)
G3	13 (24)
Estrogen receptor	
>80%	49 (90.7)
≤80%	1 (1.6)
0%	3 (5.5)
Progesteron receptor	
>80%	13 (24)
≤80%	26 (48.1)
0%	14 (26)
c-erb-B2	
Amplification	5 (9.3)
No amplification	41 (76)
Ki-67	
<20%	28 (51.9)
20-40%	15 (27.7)
>40%	10 (19)

Treatment characteristics	N° (%)
Surgery	
Quad/Lump	13 (24)
Quad/Lump + SLNB	40 (74.1)
Quad/Lump + AD	1 (1.6)
Quad/Lump + SLNB + AD	0 (0)
Systemic therapy	
Primary systemic therapy	4 (7.4)
Adiuvant systemic treatment	6 (11.1)
Endocrine therapy	42 (77.8)

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STEREOTACTIC RADIOTHERAPY IN EARLY STAGE BREAST CANCER IN NEOADJUVANT AND EXCLUSIVE SETTINGS: A SYSTEMATIC REVIEW

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Aims: Breast cancer (BC) is one of the most common tumours, better screening policies and multidisciplinary approach allow personalised treatment. Radiotherapy (RT) plays a central role in the multimodal approach in BC, and recent evidence have shown the non-inferiority of hypofractionated treatments. The aim of this study is to describe the feasibility and validity of stereotactic RT (SBRT) in BC in neoadjuvant and exclusive setting.

Method: A Pubmed/MEDLINE and Embase systematic review was conducted to assess the role of radiomics in BC. The search strategy was "breast [All Fields] AND "stereotactic" [All Fields] AND "radiotherapy" [All Fields])" and only original articles referred to BC in humans in the English language were considered.

Results: A total of 2149 studies were obtained using the mentioned search strategy on Pubmed and Embase. After the complete selection process, a total of 13 papers were considered eligible for the analysis of the results. SBRT in BC was described in 9 studies regarding neoadjuvant approach and 4 papers regarding exclusive approach.

Conclusions: Relative low toxicity rates; the reduced treatment volumes in the neoadjuvant setting and the possibility to replace surgery when not feasible in exclusive setting, resulted to be main advantages for SBRT in BC. Current evidence showed as both the neoadjuvant and the definitive settings seem to be promising clinical scenarios for SBRT especially for EBC.

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CARDIOTOXICITY ASSESSMENT AFTER ADJUVANT RADIOTHERAPY CONCURRENTLY ASSOCIATED WITH TRASTUZUMAB IN EARLY BREAST CANCER TREATED WITH OR WITHOUT ABC

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Aims: Since that the majority of breast cancer(BC) patients(pts) receive adjuvant RT and systemic treatments that can enhance cardiovascular(CV) risk, it is imperative to develop strategies to optimize radiation treatment and to reduce CV damage as a result of cardiac exposure to adjuvant treatments. Moderate deep inspiration breath hold during RT delivery helps in reducing the cardiac dose. Our study aim is to evaluate a dosimetric comparison of heart dose with active breathing coordinator(ABC) and in free breath (FB) and If ABC use impacts on global heart function in pts underwent chemotherapy(CT) and Trastuzumab(TSZ).

Method: 24 left sided BC pts who underwent BC surgery, CT and adjuvant 3DCRT. 12 pst(group1) treated in FB between 2013-2020 and 12 pts(group2) with ABC between 2021-2022 at Policlinico San Matteo were analyzed. All patients received adjuvant CT. CT regimen was epirubicin plus cyclophosphamide, followed by weekly paclitaxel for 12 weeks. According to HER2 status, all pts received TSZ except for 3 pts in group1. Pre and Post RT Left ventricular ejection fraction (LVEF) were collected for both groups. All acute cardiotoxicities were assessed according to CTCAEv5. Heart Dmean and left descending coronary artery (LADCA) Dmax were analyzed with dose/volume histograms. Patients underwent four different whole-breast adjuvant RT schemes. In group1, 2 pts (17%) received a dose of 40.05 Gy in 15 fx (HRT), 8 pts (67%) underwent HRT with SIB and 2 pts (16%) received a dose of 50 Gy in 25 fx (standard). In group2, 4 pts (33%) underwent standard treatment and 8 pts (67%) received standard treatment with boost.

Results: Mean age was 60 in group1 and 59 in group2. The level of significance was set at $P < 0.05$. Heart Dmean was 1.27Gy with ABC and 3.31Gy free breath ($P<0.0026$). LADCA Dmax was 27.41Gy with FB and 12. 38Gy with ABC ($P<0,0012$). As regard TSZ, our results for cardiotoxicity were as follows: among the 12 patients treated with FB: Grade (G) 2 in three (25%), G1 in one (8%), and G0 in 8 (66%) and one patient developed worsening LVEF with a 15% reduction. Among the 12 patients treated with ABC: G3 in one (8%), G1 in two

(25%) and G0 in 9 (75%) pts.

Conclusions: No major differences in cardiotoxicity rate were observed between ABC and FB RT. However, the use of ABC technique resulted in a significant reduction in cardiac and LADCA doses, hence, It can be considered as a promising technique for cardiac sparing especially in pts receiving CT and TSZ.

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COMPLIANCE AND FEASIBILITY OF FAST-FORWARD: THE EXPERIENCE OF AN ITALIAN INSTITUTION

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Aims: Fast-Forward (FF), according to European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice guidelines, is a valid option for Breast Cancer (BC) patients. Nevertheless, there are still many concerns about the safety and efficacy of this schedule. In this study, we aimed to collect compliance and feasibility data from BC patients who underwent FF.

Method: We evaluate acute Radiation Therapy (RT) toxicity in women treated with 26 Gy in 5 daily fractions in our institution from May 2021 to June 2022. A boost of 7.6 or 16 Gy on the tumor bed was administrated in case of Grading (G) = 3 or close (<2 mm) or positive margins. Inclusion criteria were age > 45; breast conservative surgery; T < 2, N < 1. Volumes were delineated along with Best Clinical Practice indications by "GRUPPO DI COORDINAMENTO AIRO MAMMELLA". The technique used was a 3D conformal RT. The toxicities was reported according to toxicity criteria of the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer, at the end of the treatment.

Results: Fifty-eight patients with a median age of 77 (48 – 91) years were included in the study. Thirty-three (57%) of the cases were right breast, 24 (41%) were left breast and 1 (2%) was bilateral. Thirty-seven (63%) were ductal invasive carcinomas, 13 (23%) were lobular invasive carcinomas, 4 (7%) had both the invasive and lobular components, and 4 (7%) were apocrine carcinomas. Forty-seven (80%) were G1 or G2 and 11 (20%) were G3. Median dimension of the lesions was 13 (0.4 – 45) mm and 7 (12%) patients had 1 or 2 positive nodes. Nineteen (32%), 31 (53%), 2 (4%) and 6 (11%) were Luminal A, Luminal B, Her2+ or Triple Negative, respectively. Five (8%) patients received chemotherapy, of which 1 (20%) was neoadjuvant. No patients interrupted radiotherapy, with a median overall treatment time of 5 (5 – 18) days and a median interval between surgery and the end of radiotherapy of 80.5 (46 – 217) days. One patient experienced G3 acute skin erythema, which was resolved in the next two weeks. Cases of G2 acute erythema, oedema and fibrosis were 2 (4%), 3 (5%) and 3 (5%) respectively, but no G≥2 asthenia was detected. No patients reported cardiac major events, nor pulmonary acute toxicities.

Conclusions: According to our results, FF has proven to be a safe treatment schedule in terms of acute toxicity; however, further studies are needed to assess its late effects.

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INTRAFRACTION MONITORING OF TARGET AND ORGANS AT RISK STABILITY IN LEFT BREAST CANCER BREATH HOLD RADIOTHERAPY

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Aim: The growing interest in developing techniques to minimize exposure of organs at risk during radiation therapy has led to the development of breath-holding techniques in the treatment of breast cancer, particularly in the treatment of the left breast. The purpose of our study is to determine whether the Breath Hold (BH) technique not only has the advantage of reducing damage to healthy tissue but also allows stable positioning of the target organ, breast, and organs at risk (OAR), heart and lung.

Methods: Eight patients with left-sided breast cancer were recruited. All patients underwent conformal radiotherapy 3DCRT with a TRUEBEAM linear accelerator: four of them with the Free Breathing (FB) technique, and the other four with the BH technique. Sequential portal images (cine) of the treatment fields (internal oblique and external oblique) were acquired in five consecutive sessions. We compared the cine images with the DRR images processed in the planning phase. To assess the reproducibility of the set-up, we calculated the deviation between the value measured on the cine image and the value expected by planning. In patients treated with the BH technique, we assessed the agreement between the movement of the external surrogate marker block recorded during treatment and the excursion of the internal organs planned on the DRR (R-ratio).

Results: We compared the reproducibility of the set-up planned for each organ between the BH and FB techniques using a graphical representation in which each column quantifies the average of the deviations between

the expected value and the value found during treatment. For the isocenter-skin distance and the heart, the BH technique is advantageous (Figure 1). The deflection of the marker block was found to be very similar to the actual motion of isocenter-skin distance and cardiac motion AP, so the external surrogate is a good motion index (R tends to 1). For cardiac motion CC and lung volume, the marker block performs greater motion than these organs, so its use is precautionary (R-ratio less than 1).

Conclusions: We can conclude that the use of the BH technique in left breast irradiation results not only in removal of the heart from the irradiated target, but also in a more stable intrafraction set-up of the breast target and OARs compared with FB treatments. This not only ensures greater accuracy in delivering the planned dose to the target but also saves OARs by potentially reducing the CTV-PTV margin.

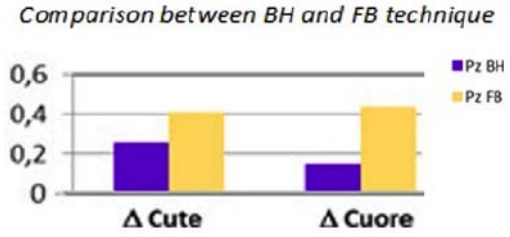

Figure 1.

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RADIATION RECALL PHENOMENON AFTER MRNA SARS-COV-2 VACCINE: A CASE REPORT

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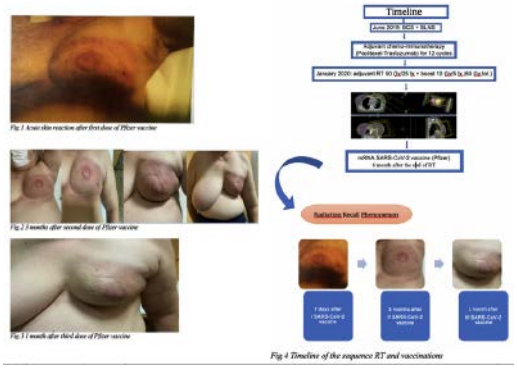
Aims: We report a case of Radiation Recall Phenomenon (RRP) after administration of mRNA SARS-CoV-2 vaccine (Pfizer) and adjuvant radiotherapy (RT) for breast cancer.

Method: A 69-year old female diagnosed with left breast DIC G3, pT1c R0 pN0(sn) M0 after lumpectomy and SNLB, subsequently received adjuvant therapy with Paclitaxel-Trastuzumab for 12 cycles and thereafter postoperative 3D-CRT with 50 Gy in 25 fractions on the residual left breast + 10 Gy boost in 5 fractions on the surgical bed. An acute Grade 1 dermatitis occurred at the end of RT. The patient had not started any new systemic medication after RT; however, she received the mRNA SARS-CoV-2 vaccine (Pfizer) 6 months after RT. One week after vaccination, the patient (pt) started to complain of acute skin reaction with burning sensation, redness and swelling in an area corresponding to the irradiation fields of the left breast. The pt had a breast evaluation which diagnosed an acute mastitis. Antibiotic, anti-inflammatory and draining therapy were prescribed without any substantial benefit (Figure 1). Three weeks later, she received the 2nd dose of the same vaccine.

Results: Due to the persistence of clinical symptoms, with left breast reddened and warm with orange peel appearance, a breast ultrasound was done which confirmed edema and phlogistic swelling of the gland (suspected mastitis carcinomatous). A subsequent skin biopsy of the left breast found "discrete interstitial inflammatory infiltrate with lymphocytes, plasma cells and fibrosclerosis". No histological signs of epithelial neoplasia were found. At a follow-up before the 3rd vaccine administration the rash persisted (Figure 2). These acute symptoms disappeared in the following months with conservative treatments. Although there is no specific test that defines RRP, its possibility should be guessed whenever an inflammation occurs after new drug/agents administration and the delivery of RT at that site within months to few years, as in our case.

Conclusions: We observed the development of RRP in 1 pt, seemingly triggered by COVID-19 vaccine. RRP is an acute self-limiting inflammatory reaction occurring after the administration of pharmacologic agents in pts who received RT weeks to few years previously. RRP is rarely reported with most of the COVID-19 vaccines and dermatitis corresponding to radiation fields is its most frequent manifestation. Patients and physicians should be aware of the potential for the RRP after COVID-19 vaccination and RT.



Figures 1-2-3-4.

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VOLUNTARY DEEP-INSPIRATORY BREATH-HOLD IN WOMEN UNDERGOING LEFT BREAST RADIOTHERAPY: FEASIBILITY AND TREATMENT TOLERANCE THROUGH A PHYSICIAN'S ANALYSIS AND PATIENT REPORTED OUTCOMES

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Aims: To retrospectively evaluate protocol's implementation, feasibility and patient reported outcomes (PROs) of deep inspiration breath hold (DIBH) using a cone-beam CT for irradiation of left-sided breast cancer.

Method: From October 2021 to May 2022 twenty-eight patients underwent adjuvant left breast/chest wall DIBH irradiation with eventual lymph nodes irradiation. Average patients' age was 52 years (40-68). Twenty patients received breast conservative surgery followed by whole breast irradiation (WBRT), three with concomitant lymph nodes irradiation. In eight patients chest wall irradiation after mastectomy was performed, seven with concomitant lymph nodes. Patients received treatments explanation without any written instructions or tutorial videos about DIBH procedure. In each case a free-breathing (FB) scan and a voluntary DIBH planning CT scan were performed. Doses ranged from 40.05 to 46Gy in 15-20 fractions respectively with 7.95Gy simultaneous integrated boost. Radiotherapy was delivered through volumetric modulated arc therapy (VMAT) by the technician's vocal instructions without a visual coach. We retrospectively analysed the average FB and DIBH scan time, the average of total scan time and the average delivery treatment time for each patient. We also explored specific PROs, obtained through a questionnaire administered at the end of treatment.

Results: The average FB scan time was 18.75s (14-27), the average DIBH scan time was 8.5s (7-10). The average of total scan time was 10 minutes (4-17). The average delivered treatment time for all patients was 12 minutes (5-55). We noticed a progressive reduction in delivered treatment time starting from the fourteenth patient. The first thirteen patients' median treatment time was longer than 25 minutes. We did not find any specific technician-related difference in terms of treatment management. Twenty-one patient did not report any treatment-related anxiety or stress, five reported moderate dyspnea or fatigue at the end treatment, and eight needed to take off face mask. Nineteen patients would have benefited from visual coaching, whereas sixteen reported little benefit from written instructions o tutorial videos.

Conclusions: In our experience DIBH is a feasible and well tolerated treatment procedure which doesn't require a long learning curve for both patients and technicians. Visual coaching could be useful to optimize the procedure, whereas pre-treatment patient's training was less appreciated.

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STOMACH AND GASTRO-OESOPHAGEAL JUNCTION DOSIMETRIC ANALYSIS IN LEFT-SIDED BREAST CANCER RADIOTHERAPY: COMPARISON BETWEEN DEEP INSPIRATION BREATH-HOLD TECHNIQUE AND FREE-BREATHING

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Aims: Adjuvant radiotherapy breast cancer is often associated with side reactions in adjacent organs including heart, skin, lungs. Although gastric side effects have not been widely analysed, digestive symptoms are often reported for patients treated with left breast radiotherapy. Deep inspiration breath-hold technique (DIBH) is known to prevent adverse cardiovascular effects and it seems to reduce also digestive toxicity. Aim of our analysis was to evaluate dosimetric impact in reducing radiotherapy dose to stomach and gastro-esophageal junction with DIBH technique in patients treated for left-sided breast cancer.

Method: Treatment plans of five women with left breast cancer were realized for both modalities: deep inspiration breath-hold technique (DIBH) and free breathing (FB). All CT-scans were acquired with empty stomach. The planning target volume (PTV) was a 5 mm isotropic expansion of the CTV with a prescribed dose of 4005 cGy in 15 fractions. All of the organs at risk and target volumes were contoured by the same physician and treatment plans realized by the same medical physicist to reduce operator variability. All treatment plans were calculated with the Raystation® 10A version treatment planning system. For both plans (DIBH and FB) the mean doses for stomach and gastro-oesophageal junction were extracted and compared using the Wilcoxon-Test. Also Dose Histogram Volumes (DVHs) for lungs, heart and left-anterior-descending coronary artery were compared.

Results: The average of the mean dose to the stomach was 5.8 cGy (range: 2.1 cGy - 152 cGy) for DIBH treatment plans while it was 113 cGy (range: 31 cGy - 235 cGy) for FB treatment plans ($p<0.001$). The average of the mean dose to the gastro-esophageal junction was 48 cGy (range: 11 cGy - 99 cGy) for DIBH treatment plans while it was 68 cGy (range: 15 cGy -129 cGy) for FB

treatment plans (p<0.001). No statistically significant differences were observed in PTVs coverage for both DIBH and FB treatment plans. Also all lung and heart constraints have significantly improved with DIBH (p<0.001).

Conclusions: Our experience showed a significant reduction in stomach and gastro-oesophageal junction doses with DIBH. Deep inspiration breath-hold technique is a valid approach for left-sided breast radiotherapy with considerable sparing of organs at risk, included stomach and gastro-oesophageal junction.

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FAIR-AC (FATIGUE IN RADIOTHERAPY AND ACUPUNTURE): A PHASE III MULTICENTRIC RANDOMIZED CONTROLLED TRIAL ON BREAST OR PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY

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Aims: Acupuncture (A) had a marked effect on fatigue (F) in cancer patients (pts), regardless of concurrent anti-cancer treatment, particularly among breast (BC) and prostate cancer (PC) patients. FAIR-AC (FAtigue In Radiotherapy and ACupunture), is a phase III multicentric randomized controlled trial that evaluates actual incidence of F in Italian BC and PC pts treated with radiation therapy (RT), and the role of A on F mitigation during RT treatment.

Methods: 400 consecutive pts affected with BC both after breast conservative surgery or mastectomy who will be referred for postoperative RT, and 200 consecutive pts affected with PC, referred for definitive or postoperative RT to three Radiation Oncology Units (in Arezzo, Grosseto and Siena) were planned to be enrolled in FAIR-AC trial. Stratification is made according to adjuvant and neo-adjuvant chemotherapy (CT) (yes/no), and PC patients according to concomitant androgen deprivation therapy (ADT) (yes/no), because both CT and ADT may cause F before the start of RT. Randomization in the 2 arms protocol (ratio 2:1) is used. In Arm 1 they are treated with "standard care" (400 pts), in Arm 2 with "standard care+A" (200 pts), to evaluate the improvement due to A respect to standard care alone. Specific and validated questionnaires investigate F and QoL.

Results: Between February 2022 and June 2022, 42 patients were enrolled (31 BC and 11 PC), randomized and their clinical data collected on a customized web-based platform. Experimental and control arms were well balanced. Breast conservative surgery was performed in 87% of BC patients. Most cases were T1-2 (87%), N0 (45%), luminal A subtype (48%), received adjuvant endocrine treatment (74%) and moderately hypofractionated breast 3DCRT (72%), for only 22% bed boost was planned. 54% of PC had high risk disease, 19% intermediate risk and 27% low risk. VMAT/ IMRT with IGRT was planned and RT volume encompassed prostate and seminal vesicles in all pts, standard doses and fractionation were prevalent. RT or RT+A and the related evaluation of side effects, QoL and F are still ongoing in most of BC and PC pts.

Conclusions: A is a safe and well tolerated treatment: if it will show activity also in RT-related F, it might be offered outside of clinical trials to prevent and reduce F to all BC and PC pts planned for RT.

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EVALUATION OF SURFACE GUIDED RADIATION THERAPY WITH VISIONRT© SYSTEM

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Aims: The accuracy and reproducibility of Surface Guided Radiation Therapy (SGRT) positioning was retrospectively investigated for the breast cancer patients' treatments, to determine if SGRT can reduce the frequency of routine image.

Methods: The patients were positioned using the skin reference surface and the live surface data with the help of infrared rays and camera of Vision-RT©, then the positioning was evaluated using standard imaging (Portal Imaging or CBCT). For each fraction the difference from VisionRT© positioning and standard imaging was recorded and then evaluated. Moreover, left breast cancer patients, candidate to voluntary deep-inspiration breath hold treatment, were monitored using highlighted ROI to control the optimal position of breathing for a correct irradiation therapy.

Results: Setup data and verification imaging were analyzed for 72 breast cancer patients (395 fractions) treated between October 2021 and May 2022. Median value of vertical, longitudinal, and lateral shifts was 1mm, with the standard deviation of 2,3mm (95% CI:0-5,5), 2,3mm (95% CI:0-5,5), 1,4mm (95% CI:0-3,7) respectively. The left breast cancer patients treated with

vDIBH were twenty-two, (123 fractions evaluated), with a median value of error of 1 mm and a standard deviation of 2,1mm (95% CI:0-5,1) in vertical shift, 2,4mm (95% CI:0-5,7) in longitudinal shift and 1,8 (95% CI:0-4,5) in lateral one's; shifts more than 5mm were in 8%,6%,4% respectively. Finally, analyzing data from patients treated in free-breathing, for 272 observations, median value of error was always 1mm in all directions, with standard deviation of 2,3mm (95% CI:0,5,5) in vertical, 2,4mm (95%CI:0-5,7) in longitudinal, and 1,3mm (95% CI:0-3,5) in lateral; shift more 5mm were 8%,6% and 1% respectively.

Conclusions: SGRT can be considered an additional safety tool, for inter-fraction motion management and for vDIBH treatment, and can provide accurate information on patient positioning prior and during the treatment. There appears to be a good correlation between SGRT and standard imaging which could reduce the frequency of imaging and therefore to associated dose.

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IMPACT OF RADIOTHERAPY TREATMENT FOR BREAST CANCER ON RESPIRATORY FUNCTION: PRELIMINARY EVALUATION OF MONOISTITUTIONAL EXPERIENCE

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Aims: The growing use of intensity modulated techniques in the treatment of breast cancer, led us to consider the impact of low dose to lungs. We preliminary evaluate impact of radiotherapy on respiratory function in breast cancer patients treated with Volumetric Modulated Arc Therapy (VMAT) on whole breast or chest wall and supraclavicular lymph nodes.

Methods: We analyzed 8 patients affected by breast cancer treated in our Institute. Adjuvant radiotherapy was delivered using VMAT technique to whole breast or chest wall and, when indicated, supra and infra-clavicular lymph nodes. A total dose of 50.4 Gy (1.8 Gy x 28), 50 Gy (2 Gy x 25) or 40.05 Gy (2.67 Gy x15) was delivered, moreover in 3/8 patients a boost on the surgical bed was added (1000-1068 cGy in 5-4 fractions). Due to heart close proximity to treatment field, 3/8 patients with left breast cancer were treated using a deep inspiration breath hold (DIBH) technique. A respiratory function evaluation with spirometry and DLCO (pulmonary diffusing capacity of the lung for carbon monoxide) was performed for all patients before radiotherapy and after one month from the end of treatment.

Results: The following parameters were measured: FVC (Forced Vital Capacity), FEV1(Forced Expiratory Volume), FEV1/FVC%, FEV1/SVC% (Slow Vital Capacity) and DLCO. The median FVC pre-RT was 3.29 lt (range: 3,79-1,85), the value post-RT was 3.38 lt (range: 3,63-1,74) with a median variation of 0,075. The median value of FEV1 pre-RT was 2,43 lt (range: 1,54-2,87) while post-RT value was 2,63 (1,44-3,04), median variation of -0,02. The median FEV1/FVC% value pre and post-RT was 77.5% and 78.5% respectively. The median FEV1/SVC% value pre and post RT was the same (76.5%). About DLCO, median values were 15.85 mL/mmHg/min and 16.5 mL/mmHg/min for pre-RT and post-RT respectively.

Conclusions: The median values of analyzed pre and post-RT parameters were similar without correlation with MLD (mean lung dose) and lung Vdose (V5,V8,V10). More patients are needed to confirm these data.

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COVID19 INFECTION AFTER BREAST CANCER RADIOTHERAPY IN PATIENT UNDERWENT NEOADIUVANT CHEMOTHERAPY E MASTECTOMY WITH IMMEDIATE RECONSTRUCTION

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Aims: Does radiotherapy used in the treatment of breast cancer increase the risk of side effects, including skin or lung sequelae, in patients with COVID-19?

Method: A 45-year-old patient with a history of hypertension underwent loco-regional breast cancer radiation therapy by Volumetric Modulated Arc Therapy (VMAT) technique and Cone-beam computed tomography-scan (CBCT) before every single fraction for online set-up correction. The target volume was the chest wall with prosthesis for immediate reconstruction after nipple sparing mastectomy. The total dose administered was 50 Gy with standard schedule of 2 Gy/fraction. Acute adverse effects experienced by patients during treatment were assessed by CTCAE v.5 criteria. In this patient were grade 2 radiation dermatitis, grade 1 esophagitis/dysphagia and grade 1 asthenia. First follow up at three months after radiotherapy treatment was negative for any grade toxicities with complete recovery. 15 days after radiotherapy follow up Covid-19 infection occurred with simultaneous appearance of symptoms on irradiated site breast-implant such as edema and erythema as if post-actinic side effect. Ultrasound detects the presence of periprosthetic fluid that was drained. Topical and antibiotic therapy were done. After one month the regression of symptoms were obtained as well as Covid-19 infection resolution.

Results: In our clinical case COVID-19 infection was

related to the appearance of skin reaction as if it were a post-actinic side effect at previous irradiated breast implant chest-wall despite literature data confirmed that COVID-19 does not appear to increase the early adverse effects of radiotherapy.

Conclusions: In our experience side effects apparently related to radiotherapy by location and type were instead found to be related to COVID-19 infection, therefore in suspicious clinical situations further investigations were to be evaluated.

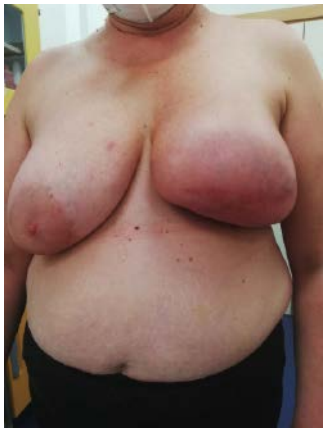

Figure 1.

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STEREOTACTIC BODY RADIATION THERAPY FOR BONE METASTASES IN OLIGOMETASTATIC BREAST CANCER

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Aims: Breast cancer is the most common cancer affecting women worldwide, with bone metastases presenting as the most common site of disease recurrence. Bone metastases secondary to breast cancer negatively impacts patients survival, mobility and quality of life. In this study we assessed the efficacy of stereotactic body radiation therapy for bone in terms of local disease control in breast cancer patients with oligometastases.

Patients and Methods: We retrospectively analyzed 17 breast cancer patients, aged between 25 and 86 years, treated with SBRT for bone from January 2020 to Dicember 2022. The patients were classified based on intrinsic biological subtypes in Luminal A (26%), Luminal B (71%) and triple-negative (3%), while based on histology in infiltrating ductal (94%) and lobular (6%) carcinoma. The stereotactic body radiation therapy for bone was used as the only treatment in 9 patients; the other 8 patients also received palliative treatment. It was performed at a median total dose of 26 Gy and median daily dose of 7 Gy.

Results: The patients enrolled in this study mostly had one to three lesion(s) represented site was pelvis bone. Median follow-up after bone SBRT was 11 months (range 1-20 months). Local recurrence was observed in only one patient, with disease-free interval at the same site of 14 months. In 11 of 17 patients the disease did not appear in any other bone site besides the one treated site, while in 6 patients it appeared in other untreated bone sites.

Conclusions: The bone SBRT in oligometastatic patients was able to achieve higher local control rates, as well as to provide longer progression-free survival therefore, this may be an effective treatment modality.

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ULTRAHYPOFRACTIONATION RADIATION THERAPY IN BREAST CANCER IN "COVID-ERA"

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Aims: To evaluate acute and late skin toxicity in ultra-hypofractionation RT in breast cancer. The conventional or hypo-fractionation often was not performed due to "COVID-19 era", we choose the ultra-hypofractionation (1 fx/week for 5 weeks) in pts with difficulties in reaching our center.

Method: From April 2020 to April 2022, we enrolled 10 pts, median age 76 years, with early stage breast cancer, PS 0-1 ECOG. All pts performed BCS, and histologically were invasive breast carcinoma- LUMINAL A, no pathological nodes. 8 pts had right breast cancer and 2 had left. To evaluate acute and late skin toxicity, we performed a clinical visit after 1 mth and then at 3-6-12 and 24 months. All patients were treated with LINAC ELEKTA Sinergy in 3D-cRT-6MV- with personalized immobilization device, PTV is whole breast and OARs: lungs and hearth (in left cancer breast). **Total dose was 25 Gy/5 Gy fx once a week, isodose 95% according ICRU and evaluated OARs QUANTEC-according.** Skin toxicity was evaluated with RTOG-scale.

Results: Since 2020 we treated 10 pts with ultra-hypofractionation, all pts completed the radiotherapy. All pts performed a clinical visit 1 mth after radiation therapy, 9 pts after 3 mth, 6 pts after 6 mth, 5 pts after 12 mth and 1 pt after 24 mth. On the day of discharge, 6 pts had mild skin erythema in the irradiated area (G1), the other pts did not show signs of skin toxicity (G0). VISIT 1 (After 1 mth): 6 pts had mild erythema (G1); 4 pts had no acute toxicity G0. VISIT 2 (After 3 mth): 4 pts had acute

skin toxicity G1: faint erythema; 5 pts had no skin toxicity G0. VISIT 3 (after 6 mth): 3 pts had late skin toxicity G1: pigmentation change; 3 pts had no skin toxicity G0. VISIT 4 (after 12 mth): 2 pts had late skin toxicity G2: breast induration; 2 pts had late skin toxicity G1: pigmentation change; 1 pt had no skin toxicity: G0. VISIT 5 (after 24 mth): 1 pt had late skin toxicity G2: breast induration. No toxicity G3 treatment-related was observed.

Conclusions: Since 2020 with pandemic era, access to care has been conditioned by the state of emergency. Elderly pts with breast cancer often had poor compliance to conventional or hypo-fractionated protocol: the risk of a non-optimal RT treatment was high. In our experience, the ultra-hypofractionation is safe. This type of treatment represents a bridge between the difficulties of pts in this pandemic era and the need to guarantee the correct therapeutic path to all.

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NIPPLE/SKIN SPARING MASTECTOMY: CONSERVATIVE CHARACTER *VS* RISK OF LOCAL FAILURE

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Aim: In non-metastatic breast cancer (NM-BC), Nipple Sparing Mastectomy (NSM) and Skin Sparing Mastectomy (SSM) are two innovative surgical techniques which over the years have given results, in terms of efficacy, comparable to the radical mastectomy. However, due to their more conservative character are associated to the persistence of mammary tissue resulting in an increased risk of local failure (LF) especially when it is larger than 5mm. Role of radiotherapy treatment post NSM/SSM (PMRT) is currently controversial. We aim to assess the persistence of mammary residue, evaluable through ultrasound, in patients who underwent to NSM and SSM.

Methods: From 2015 to 2022 we enrolled 15 patients (from different centers) with NM-BC, localized or locally advanced, who underwent to NSM or SSM. Post surgery mammary glands Ultrasound was obtained.

Results: Between all 15 examinated patients, neoadjuvant and adjuvant systemic treatment (chemotherapy and /or hormonotherapy) were performed in 7 (46,66%) and 8 (53,33%) patients, respectively. 6(40%) patients underwent to NSM and 9 (60%) to SSM. Mammary gland ultrasound showed the presence of mammary gland residue in 86,66% (13/15) of patients. Patients with post surgical residue have been treated with radiation therapy.

Conclusion: Our preliminary results demonstrate that despite NSM and SSM represent two cutting-edge techniques in surgery and oncology, and are equipped with a more conservative approach than radical mastectomy, in a high percentage of cases there is a post-surgical mammary gland residue, which is also related to an higher risk of LF. Ultrasound evaluation, after NSM or SSM, should be considered in clinical practice in order to identify glandular breast residue which could suggest a radiotherapy adjuvant treatment.

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COPING WITH MODESTY AND NUDITY DURING RADIOTHERAPY FOR BREAST CANCER: A MULTICENTRIC STUDY

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Aim: The relationship with the body may change for many breast cancer (BC) patients who have undergone oncological treatments. Modesty and body confidence can be affected too, leading patients to psychological distress. Aim of this study is to present the results of a multicentric prospective observational study, aimed to describe how nudity and modesty are perceived by BC patients undergoing adjuvant RT.

Method: Modesty was evaluated by means of a 11 questions self-test questionnaire (9 yes/no and 2 open), developed for the specific purpose through a Delphi consensus run by a multidisciplinary board of experts in the field of BC RT, psycho-oncology, patients advocacy and RT delivery. Table 1 reports questions list. The questionnaire was administered to consecutive female BC patients undergoing RT during first week of treatment in 3 centers in central (site A), southern (site B) and northern (site C) Italy.

Results: 537 patients have been enrolled since August 2020 in 3 Italian institutions (center A 196, center B 180, center C 161). Patients mean age was 56±14 years. 75.2% of patients stated not to be embarrassed being bare chest during RT. 78.2% stated to be comfortable being undressed in front of healthcare workers, while 40.8% admitted that exposing themselves has become more difficult after surgery. Religious feelings, RT staff sex and age did not appear to influence patients' perceived overall comfort. Interesting suggestions were collected from free text answers, such as: presence of at least one female member in the staff during RT sessions; presence of the same staff; reducing distance from dressing room to treatment couch; provide a gown to cover with until reaching the treatment

couch; if possible, covering breast during treatment delivery. Empathy of the RT staff; listening to music and "ice-breaking exhortations" have been identified as strength points of the relationship of care. The attendance of male only RT staff and the simultaneous presence of different healthcare workers in the therapy room, on the other hand, reduced patients' comfort. Results are listed in Table 1.

Conclusions: Nearly 25% of BC patients can experience modesty issues during RT. This can be balanced by staff professionality and empathic approach. Suggestions offered by patients gave insights how to improve patients comfort in treatment room. Modesty and nudity perception represent interesting topics to be explored with the aim to further promote patients wellbeing during treatment.

Table 1.

Questions	Answers		
	Yes	No	Preferred not to answer
Do you feel comfortable when you are without clothes during RT?	404 (75.0%)	131 (24.6%)	2 (0.4%)
Do you have any problem to show you undressed in front of strangers?	218 (40.5%)	318 (59.3%)	1 (0.2%)
Do you have any problem to show you undressed in front of healthcare workers?	420 (78.2%)	117 (21.8%)	0
Do you feel it is more difficult to show you undressed in front of strangers after surgery?	318 (59.1%)	218 (40.7%)	1 (0.2%)
Do you feel more comfortable when you meet healthcare workers of your gender in treatment room?	332 (61.8%)	205 (38.2%)	0
Do you feel more comfortable when you meet healthcare workers of your age in treatment room?	442 (82.3%)	95 (17.7%)	0
Do you ever feel uncomfortable being without your clothes during therapy?	431 (80.3%)	106 (19.7%)	0
Do you have religious reasons due to which you prefer not to show you undressed in the presence of strangers?	516 (95.1%)	11 (3.0%)	10 (1.9%)
Do you feel your sexuality will be overall influenced by this experience?	412 (75.7%)	115 (22.4%)	10 (1.9%)
Did you report to the in-room staff if you feel comfortable without your clothes during therapy?	Open Question		
Do you have any suggestions to better manage this aspect?	Open Question		

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USE OF CHABNER XRT® RADIATION BRA IN LARGE-BREASTED PATIENTS: A PRELIMINARY EXPERIENCE

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Aims: Despite modern techniques, in the Radiotherapy (RT) of breast cancer patients (pts) undergoing conserving surgery, large pendulous breast often presents problems during simulation, planning and treatment, including increased skin toxicity and lung and heart dose. We report our experience with large pendulous breasted pts treated with Bra during RT and its effect on treatment reproducibility, acute skin toxicity and lung and heart dosimetry.

Method: From August 2020 to March 2022, 10 large-breasted pts (5 right and 5 left) underwent RT after breast conserving surgery. During simulation, pts put on Chabner XRT® Radiation Bra (Bra) custom-fit adapted to ensure that the breast tissue was contained entirely within the Bra cup (Figure 1). The shoulder straps have been adjusted and all points of Velcro® attachment have been indexed. Thermoplastic polyurethane windows allowed visibility of skin and bony landmarks essential for repeatable position. Two mm slices-Computed Tomography scan was acquired with and without Bra in supine position on a breast board immobilization device, with both arms raised above the head. RT was performed using 3-dimentional RT (3DCRT) in 5 pts and volumetric modulated Arc therapy (VMAT) in 5 pts. In 3 pts with unfavorable anatomy or comorbidities deep inspiration breath hold (DIBH) technique was used. All pts received 40,05 Gy in 15 fractions to whole breast (WB) with a sequential or simultaneous integrated boost. Selected dose constraints were: Dmean ≤ 5Gy, V8Gy ≤ 30%, D5% ≤ 16 Gy to the heart; V16Gy ≤ 20%, V8Gy ≤ 35%, V4Gy ≤ 50% to the ipsilateral lung. Toxicities were evaluated using CTCAE 5.0 scale.

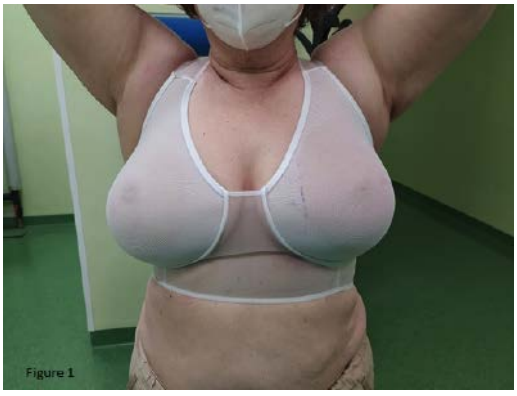

Figure 1.

Results: 3DCRT or VMAT technique planning and Bra device allowed dose homogeneity, less lateral breast displacement with less heart and lung involvement, compared to plan without Bra. The dosimetric parameters were in all pts: heart V8Gy ≤ 8%, D5% ≤10 Gy Dmean ≤ 4 Gy; ipsilateral lung V16Gy ≤ 19%, V8Gy ≤ 33%, V4Gy ≤ 44%. Daily IGRT showed optimal reproducibility. RT was well tolerated: all pts presented Grade 1 fatigue, disappeared after 1 month of follow-up; 8 pts Grade 1 and 2 pts Grade 2 erythema.

Conclusions: In our preliminary experience, the use of Bra improved simulation, planning, daily reproducibility and cosmetic outcome. This device application also reduced dose to heart and ipsilateral lung. Further cases are needed to confirm its effectiveness in treatment reproducibility and dosimetric parameters improvement.

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SINGLE-CENTRE IMPLEMENTATION OF RADIOTHERAPY-DEDICATED BRA FOR LARGE AND PENDULOUS BREAST

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Aim: Dose conformality and homogeneity is commonly obtained in breast 3D-CRT field-in-field radiotherapy but large and pendulous breast can be challenging due to large inframammary fold and lateral displacement. This affects the risk of skin toxicity and organs at risk (OARs) doses. This study aims to evaluate the geometric and dosimetric effects of bra application during radiotherapy for large and pendulous breast.

Method: Six patients underwent breast radiotherapy with a radiation bra between October 2021 and May 2022, 4 of them with a FAST-forward (FFW) schedule and 2 with the conventional hypo-fractionated scheme. According to the patient's chest and cup size, a suitable bra was selected and 2 CTs (without (NB) and with bra (WB)) were acquired. Measured parameters included the nipple-to-pectoral muscle distance (NPD), the maximum medio-lateral thickness (MLT) along tangential fields, the CTV volume and its conformity (CI) and homogeneity indexes (HI). The OARs were the ipsilateral lung and the heart.

Results: The bra sizes ranged from 4 to 9 with optimal patients compliance. While the MLT resulted constant, the use of the bra provided a decrease in the median NPD (NB 8.2 cm; WB 7.0 cm) and the median CTV (NB 1019.5 cm^3; WB 890.5 cm^3). While the target coverage was maintained (V95%: NB 98.9%; WB 99.3%), the median volume of the 105% and 107% isodoses without and with the bra was 13.0 cm^3 and 1.2 cm^3, and 0.5 cm^3 and 0.0 cm^3, respectively. This led to a 0.6 median CI value for both NB and WB but to an improvement in the HI (NB 0.09; WB 0.07). Any clinically relevant variations in lung and heart doses were registered. The WB plan was always chosen over the NB plan and all treatments were successfully delivered with a daily pre-treatment CBCT correction without affecting the department's daily routine. No toxicities have been registered.

Conclusions: The bra implementation was associated with improved geometric and dosimetric planning parameters: higher and properly positioned breast guaranteed a smaller CTV and reduced hot spots. In particular, it allowed offering the FFW schedule to patients whose breast volume would have not permitted a sufficient dose homogeneity. A higher number of patients will allow defining the best cut-off parameters in the choice to use the bra and to confirm its dosimetric impact. The clinical follow-up will give fundamental feedback on eventually reduced toxicities thanks to a more homogeneous dose distribution.

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MAY OLAPARIB COULD BE "UNSAFE" DURING ADJUVANT RADIATION THERAPY FOR BREAST CANCER? A CASE REPORT

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Aim: PARP1/2 inhibitors can selectively target tumor cells with defects in BRCA1 or BRCA2 suppressor genes that normally maintain the integrity of the genome by mediating a DNA repair process, known as homologous recombination. Olaparib is used for the treatment of malignances with a mutation of BRCA 1 or 2, like ovarian or breast cancer.

Methods: A 74 years old woman with a metastatic ovarian cancer from 2011 and a vesical sarcomatoid carcinoma from 2013 developed in 2020 a left breast cancer (ductal carcinoma pT1bpN0(i-), ER 95%, PgR 0%, ki67 35%, HER2 2+, FISH not amplified). The woman, after a complete remission, is in maintenance therapy with Olaparib. Instead of a BRCA1 mutation (exon 11), she underwent a conservative surgery with sentinel node biopsy and after multidisciplinary discussion we decided for Adjuvant Ormonotherapy with Anastrozole and Radiotherapy with ipofractionated schedule (total dose 30 Gy, 6 Gy/fraction, 5 fractions, 1/week) from december 2020 to january 2021.

Results: Acute toxicity after radiotherapy was minimal, with a erythema G1. Late toxicity develops 6 months after the end of radiation therapy with edema and fibrosis with deformity G3 from the axilla to all the breast (see picture) and a progressive retraction of the tissue and mastitis. All the radiological, haematological and bioptical exams were negative for progression disease. The woman was treated with different antibiotics, unsuccessfully. We decided to treat the patient with oral and local anti-edematous with a partial reduction of the local symptoms after 1 year of treatment (Figure 1).

Conclusions: In the literature a phase 1 study with

breast radiotherapy and concomitant Olaparib shows little adverse events, still reporting a case of fibrosis and deformity of the breast. Concomitant radiation therapy and Olaparib must be evaluated case by case, with a tempestive treatment of the local toxicity.

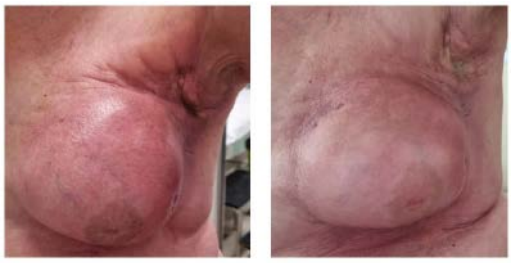

Figure 1.

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NEOPRENE UNDERWEAR TOP OR BRA ON CHEST WALL IN POSTMASTECTOMY ADJUVANT RADIOTHERAPY: DOES IT WORK AS BOLUS?

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Aims: The need for bolus on chest wall in postmastectomy radiotherapy is still questioned. It is a tissue equivalent material that shifts the 95-100% isodose line towards the skin and subcutaneous tissue but there are difficulties on set up reproducibility and dose coverage uniformity in case of expanded chest wall with prothesis reconstruction or irregular surfaces. Neoprene clothes present in the market could be a good solution as we found in our preliminary experience .

Methods: Five patients eligible for adjuvant postmastectomy radiotherapy were identified. Two patients needed skin dose coverage because has subcutaneous R1 after skin sparing mastectomy with spherical shaped prothesis reconstruction; one patient had a thin thickness chest wall; the other two patients had pT4 staged breast cancer. A neoprene 3-5 mm thick tank top or bra as bolus were worn on the chest wall in all of them. To assess the dose delivery trough the clothing on the external surface, the dose was measured with a ionizing chamber; then Gafchromic films were applied on 6 points of the chest on an anthropomorphic chest phantom wearing the neoprene clothing to assess dose coverage and homogeneity distribution. Then the plan was delivered to the patients. CTV consisted of the chest wall with or without reconstruction defined according EORTC guidelines with the external margin cropped 2-3mm from the external contour including the neoprene border. IMRT or VMAT 6 MV photon beams were applied; PD was 50 Gy with standard fractionation.

Results: All measurements showed a dose delivery trough the neoprene clothing. Gafchromic dosimetry on chest phantom showed a dose distribution on the esternal surface with more homogeneity and less hot spot doses. The 99.6% of PTV 50 received the 95% of the prescribed dose (PD Gy); the D100 (prescribed dose 100%) was delivered to the 53.7% of volume; no 107% of the PD was recorded. By the comparison between the measured and calculated dose on Gafcrhomic films there was a difference of less then 5%. Setup errors were less than 2 mm on daily CBCT. G2-G3 erythema was the main acute side effect occurring in the last week of treatment.

Conclusions: Neoprene clothing like tank top or bra worn as customized bolus in postmastectomy adjuvant radiotherapy works well leading to a better homogeneity and delivery dose, coverage of the entire chest wall surface as well as robustness to minimize setup errors.

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REPRODUCIBILITY OF IMAGE-GUIDED DEEP INSPIRATION BREATH HOLD FOR LEFT-SIDE BREAST CANCER

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Aims: To quantify positional reproducibility and normal-tissue sparing in patients undergoing left breast radiotherapy (RT) with deep-inspiratory breath-hold (DIBH)

Method: A patient was treated with hybrid 3 dimensional conformal RT/Volumetric Modulated Arc Therapy DIBH technique for left breast cancer. Patient received 15 fractions of 2,7 Gy (total dose 40,5 Gy). Cone-beam computed tomography-scan (CBCT) performed during DIBH was used for online manual set-up correction. Reproducibility of the DIBH was also monitored with 2D-fluoroscopy acquired after online CBCT at the angle of the first static treatment beam. It was retrospectively evaluated inter-fraction variability between simulation CT and daily CBCT measuring offline set up variations and V20 values of ipsilateral lung. It was also identified a landmark (surgical clip) as an organ surrogate for the left breast and its displacement during 2D-fluoroscopy was recorded frame by frame. To evaluate the quality of the final set up position the last frame 2D-fluoroscopy DRR was compared to the corresponding simulation CT DRR by manual match.

Results: Fifteen CBCT were evaluated. The mean correction found was 0.47cm ± 0.29cm, 0.30cm ± 0.31cm, -0.16cm ± 0.28cm, 0.33° ± 0.70°, -0.56° ± 0.73°, 0.01° ± 1.26° for vertical, longitudinal, lateral, pitch, roll

and rotation respectively. Ipsilateral lung V20 in simulation CT was 311 cc. The mean V20 in CBCT was 325 cc (range 288-365cc) equal to average percentage variation of 4.5 % than respect to simulation CT. In regard to 2D-fluoroscopy analysis no movement of landmark greater than 1mm was found. The mean residual error between kV fluoroscopy and simulation CT DRR occurred was 0.02cm ± 0.11cm, 0.02cm ± 0.17cm, 0.01cm ± 0.08cm, 0cm ± 0.26cm, 0cm ± 0cm, 0.1cm ± 0.14cm for vertical, longitudinal, lateral, pitch, roll and rotation respectively.

Conclusions: In our experience image-guided DIBH technique is a feasible irradiation method with small set-up variability and optimal organ motion reproducibility.

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A DEDICATED WEB PLATFORM DESIGN FOR FAIR-AC (FATIGUE IN RADIOTHERAPY AND ACUPUNTURE), A PHASE III MULTICENTRIC RANDOMIZED CONTROLLED TRIAL

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Aims: Activation of a web platform for the management of a phase III multicenter clinical trial (FAtigue In Radiotherapy and Acupunture, FAIR-AC study) investigating the impact of acupuncture on fatigue of patients on radiotherapy for prostate or breast cancer. The platform is accessible on the internet in compliance with the GDPR legislation. The Istitute for Cancer Research, Prevention and Clinical Network-ISPRO of Florence is the Clinical Data Management Coordinator, the three Radiation Oncology Units of Arezzo, Grosseto and Siena are the Experimental Centres for recruitment, treatment and follow up of patients.

Methods: The customized development of the platform was based on latest generation Microsoft technology, fit for even small-sized devices. The design of the sequence of participation in the study was carried out on the basis of the specific requests of the Researchers. A test platform is provided to verify any new features before releasing them into production. The automatic randomization design is based on the dynamic method of minimization, according to https://www.evidence.it/articoli/pdf/2009_1_2.pdf.The interface was developed with Microsoft technology. Platform WEB e DB: OS:Windows server 2014, WEB Server: IIS 8, DB: Sql Server 2012, Framework: ASP.NET CORE 5.0.

Results: The web platform included both an automatic randomization workflow in the treatment arms "Standard" and "Standard + acupuncture" and a data collection software. The platform is currently used by 15 Specialized Operators based on roles with related functions that can be summarized as: insertion and updating of data (clinical data, toxicity of treatment, quality of life and fatigue validated questionnaires, acupuncture data), study progress control, data export and processing. Each user who accesses the platform has a nominal account. Database protection is guaranteed by the daily cumulative backup. The modules can be added or modified even during the study on the basis of the Researchers' requests. The online system is anonymized. In the developed platform, no sensitive data is associated directly with the participant. Personal data and the codes to allow the association with clinical data are reported by Researchers only on the paper used as clinical records.

Conclusions: The system is currently operational and can be easily accessed with a personalized account at the following URL https://fair-ac.it:8443/. The data analysis can be performed live on the data present in the DB through direct connection to SAS and R.

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POOR ACCRUAL TO FAI-A-C PROTOCOL: REASONS

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Aims: We want to understand why many patients reject the proposal to be enrolled in a randomized study designed to investigate the incidence of fatigue (F) and the role of acupuncture (A) in relieving F in patients (pts) treated with radiotherapy (RT) for breast cancer (BC) and

prostate cancer (PC).

Methods: From January 2022 the recruitment phase began in the prospective randomized phase III study which involves the enrollment of 400 pts diagnosed with BC undergoing conservative surgery or mastectomy who must undergo adjuvant RT and 200 pts diagnosed with PC who must undergo radical RT or adjuvant or salvage RT. Enrolled pts were randomized into two groups). In group 1 the pts will be treated with "standard care" (300 pts), in group 2 they will be treated with "standard care + A" (300 pts), in order to assess whether A determines benefits in terms of fatigue. In enrolled patients, fatigue and quality of life were assessed before, during and after treatment. While the pts, who refused enrollment, were administered a multiple choice questionnaire: 1) lack of confidence in acupuncture (1); 2) poor knowledge of acupuncture (2); 3) belonephobia (3); 4) other (4); to understand the reasons for refusing to participate in the study.

Results: The study, from January to May 2022, was proposed at 129 pts (67 males and 62 females), only 79 pts were randomized (45 pts diagnosed with PC and 34 pts diagnosed with BC), while the remaining 50 pts refused to join the study (22 pts with PC and 28 pts with BC). Questionnaire results show that 30% (15 pts) of patients responded 1, 40% (20 pts) responded 2, 20% (10 pts) responded 3, and 10% (5 pts) responded 4.

Conslusions: Preliminary results show that many patients refuse to join the study due to lack of confidence and knowledge of A, so better communication and disclosure of the benefits of A and the few side effects will be needed in the future.

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ACCELLERATED PARTIAL BREAST REIRRADIATION AS RESCUE INSTEAD OF MASTECTOMY IN RECURRENT BREAST CANCER

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Aims: Mastectomy is the standard of care for recurrent breast cancer after conservative surgery and adjuvant radiotherapy. However, accelerated partial breast reirradiation (APBRI) following lumpectomy could be a viable option to offer in case of mastectomy refusal. This analysis includes few patients that refused mastectomy and received APBRI with external beam radiotherapy (EBRT). We report acute and late effects further locoregional and cosmetic outcomes.

Methods: From 2019 to 2022 five patients with recurrent ipsilateral breast cancer after breast conserving surgery, were treated with salvage lumpectomy followed by adjuvant APBRI with EBRT. 3D-conformal RT and IMRT were adopted in 3 and 2 patients respectively. Eligibility criteria included a recurrent and unifocal tumor, less than 3 cm, wide margins, more than one year after radiotherapy and a lumpectomy-residual breast ratio less than 30%. Mean age was 60 years (45-70); mean time to recurrence was 6 years (5-15 years). After lumpectomy with wide margins and clips to delineate surgical cavity, patients received 1.5 Gy twice daily for 30 treatments during 15 days to a total dose of 45 Gy. Dose prescription and OAR's dose constraints were applied according the NRG Oncology RTOG 1014 study. CTV was the lumpectomy cavity with 15 mm; 5 mm was provided under the skin and over the chest structures. A 10 mm isotropic margin generated the PTV. Treatment was delivered within maximum 8 weeks after lumpectomy. Local control (LC), overall survival (OS), disease free survival (DFS) as well as toxicities and cosmetics effects were evaluated in this analysis.

Results: After a median follow-up of 20 months (6-26 months), no regional or distant relapse was verified, resulting in a median LC rate, DFS, OS 100% at 18 months. Regarding toxicity, 3 patients (3/5) developed adverse events (CTCAE grade </= 2) with fibrosis in 3 patients, hyperpigmentation in 2 and telangiectasia in 1, respectively. No patients showed high grade (CTCAE >/= 3) adverse event and all patients had good cosmetic outcomes.

Conslusions: Among APBI technique (EBRT, intraoperative RT, brachitherapy), APBRI with EBRT after second lumpectomy in recurrent ipsilateral breast cancer is safe and effective option for breast sparing.

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HYPOFRACTIONATED POST-OPERATIVE RADIATION THERAPY FOR EARLY BREAST CANCER

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Aims: The purpose of the study was to evaluate the acute and late side effects of skin, cosmetic result, and disease control in patients with breast cancer who received adjuvant hypofractionated radiotherapy.

Methods: from april 2014 to april 2022, in our center, were treated 364 women with breast cancer who had undergone conservative surgery. The median age was 61 (range 35-89). 325 patients (90%) had a histological report of invasive ductal carcinoma, 21 patients (6%) had a histological report of invasive lobular carcinoma, 8 patients (2%) had a histological report of invasive papillary carcinoma, 5 patients (1%) had a histological report of invasive tubular carcinoma, 5 patients (1%) had a histological report of mucinous carcinoma. 307 patients (84%) were in T1 stage and 57 patients (16%) were in T2 stage, 44 patients (12%) had N1 positive lymphnode. All patients were treated with external beam radiotherapy for a total dose of 42.40 Gy, with 2.65 Gy dose fraction for 5

days a week.

Results: All patients completed radiotherapy. 273 patients (75%) presented acute toxicity of Skin of Grade 1 and 76 patients (21%) presented acute toxicity of Skin of Grade 2. In a 20.8 months average follow-up: 19 patients (5%) showed late skin toxicity, in 10 patients (3%) was observed distant recurrence and 4 patients (1%) showed local disease.

Conclusions: In our study we didn't find any significant acute skin effects such to invalidate the therapeutic choice. Was observed low incidence of late skin toxicity with satisfying cosmetic outcome. Hypofractionated adjuvant radiotherapy has been proved to be an appropriate treatment choice for control desease.

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TRASTUZUMAB-INDUCED RADIATION RECALL DERMATITIS (RRD): A CASE REPORT

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Aims: We report the RRD phenomenon triggered by trastuzumab in a woman undergoing breast-conserving therapy five months after radiation therapy. RRD is well recognized in the medical world but poorly understood and has been defined as the "recalling" by the skin of previous radiation exposure in response to the specific drugs administered from days to years after exposure to ionizing radiation. RRD is characterized by an inflammatory response localized to the irradiated body site. Although the precise mechanism underlying radiation recall dermatitis is unknown, it has been proposed that stem cell depletion, increased local vascular permeability, overexpression of transforming growth factor β1 (TGF-β1), or the expression of inflammatory cytokines may cause this condition.

Methods: A 59-year-old woman was treated for breast cancer and subsequent sequential chemotherapy and radiotherapy after conservative surgery. The patient had comorbidities such as Hashimoto thyroiditis, Behcet's disease, acute joint rheumatism, and a previous hysteroannessiectomy for ovarian cancer. In December 2020, she underwent left conservative surgery with ipsilateral axillary dissection, adjuvant chemotherapy, and trastuzumab (Herceptin®). In June 2021, she underwent a hypofractionated radiotherapy RT treatment (40.05Gy/15fr.) on the left breast with the breath-hold technique. The treatment was well tolerated with minimal cutaneous toxicity evidenced as mild erythema (grade 1 using CTCAE, v5.0) with a soothing moisturizer. After five months, the patient experienced marked erythema in the irradiated site and the ipsilateral forearm.

Results: A topical corticosteroid application and oral second-generation antihistamine treatment were started with close observation of reactions. The patient did not stop programmed trastuzumab administration; during therapy, the erythema and the itching were alleviated. The skin change was fully resolved only after three months from the end of the planned treatment.

Conclusions: The incidence of this disorder is predicted to increase in the future, primarily due to the interactions with various bioogical drugs. Therefore, when erythema appears during post-operative follow-up at an area that coincides with the irradiated site, a radiation recall dermatitis must be suspected.

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PRIMARY ECTOPIC AXILLARY BREAST CANCER (EBC): A CASE REPORT

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Introduction: Ectopic breast Tissue is present in 2 – 6% of women and can be found along the mammary line. The axilla is the most common site, while the sternum area, the infraclavicular region, the epigrastium and the vulva have also been described. EBC represents an uncommon disease accounting for 0.3% of all breast cancer. Surgical treatment consists of wide excision of tumor with lymphadenectomy. Concerning the adjuvant treatment of EBC, it has the same indications as breast cancer. There are many controversies about target irradiated volume: some authors considered ectopic breast, chest wall, internal mammary nodes while other authors considered only tumor bed. In this case report we present a patient with EBC treated at our institution.

Method: A 68 years old woman presented a mass in the left axilla, showed by ultrasonograpy from June 2018. In August 2020, after a progressive growth of the lesion , a breast magnetic resonance (MRI) was performed and showed a nodule measured 25 mm. In September 2020, local excision was performed which revealed "Invasive ductal carcinoma" (CDI), triple negative with Ki 67 75%. The patient's addominal ultrasonography, thoraco-abdominal computed tomography and whole bone scan were negative for metastasis disease. In October 2020 a new MRI was performed and showed a residual disease of 10x6 mm in left axilla. Biopsy was performed which confirmed CDI G3. On 22/10/2020 the patient underwent to reexcision and left axillary dissection. The histological type was CDI G3 and it was staged pT1apN1a(1/15)G3.

Results: The patient was referred to our radiation department in Barletta. She received chemotherapy from December 2020 to June 2021 with 4 course of epirubicina and cyclofosfamide x4 and weekly taxolo for 12 weeks. Radiotherapy was delivered at total dose of 50 Gy without boost, including tumor bed as volume, according to the literature. During treatment no toxicity was reported, according to the CTCAE v. 4.0 scale. After 1 year of

follow up the patient is in good performance status without any evidence of local recurrence or distant metastasis.

Conclusions: Conclusive date regarding recurrence and survival in patients with EBC are lacking due to its rare incidence. Further studies are required to give a higher grade of recommendation for its management and to understand the optimal Rt treatment volumes to avoid overtreatment or unnecessary toxicity to the patients.

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THE RADIATION ONCOLOGIST'S ROLE IN THE BREAST UNIT TEAM UP-FRONT DISCUSSION: OUR EXPERIENCE

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Aim: The radiation oncologist's role in the Breast Unit (BU) team got a decisive impact in the up-front making decision process in case of several breast cancer (BC) scenarios needing a tailored and organized combination with surgery and radiotherapy in case of mastectomy or breast conserving surgery (BCS) whatever.

Methods: From 2021-2022 more than 100 breast cancer patients (pts) were discussed in an up-front multidisciplinary meeting to customize treatment sharing the decision with radiation oncologist Among them, 40 pts had a change of the initial therapeutic program in light of these scenarios: ICD located in the RT field (a), autoimmune diseases (LES and sclerodermia, (b), arm impairment in the affected breast side (c), mastectomy and chest wall implants with immediate or delayed reconstruction after neoadjuvant chemotherapy (d) ; partial breast RT for recurrence (e); BRCA, TPA, ATM deleterious mutations (f).

Results: In the majority of cases the initial decision was changed on the basis of the radiation oncologist's point of view. Mastectomy without adjuvant RT was advised in 22 patients with early BC in case of ICD in the side of affected breast (a), in shoulders impairment (b), deleterious mutations while in scenario (c) adjuvant RT was prescribed after a BCS in non active autoimmune disease for 3 pts. In case of mastectomy after neoadjuvant chemotherapy, a delayed chest wall reconstruction with temporary implants was planned in 10 cases showing advanced breast cancers needing adjuvant RT on chest wall and nodal areas. In 5 patients with recurrence PBI was chosen instead of savage mastectomy.

Conclusions: In the BU team discussion the radiation oncologist role is an emerging and relevant protagonist in the up-front tailoring making decision process.

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A COMPREHENSIVE MULTIVARIATE ANALYSIS OF MULTIPLE SYSTEMIC INFLAMMATION MARKERS IN RECTAL CANCERS UNDERGOING NEOADJUVANT CONCURRENT CHEMORADIATION

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Aims: Interest in radiotherapy about markers of systemic inflammation has spread due to their value in predicting pathological complete response (pCR) and outcomes in rectal cancer (RCa) patients (pts). However, in most studies only one index was analyzed. Aim of this study is to evaluate a wide range of inflammation indices including known prognostic factors.

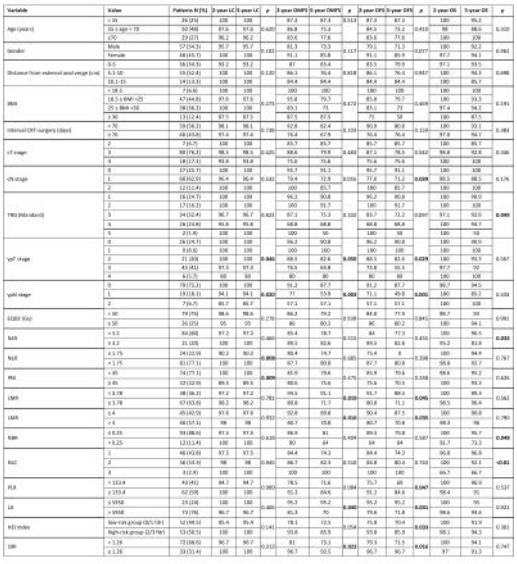
Methods: We retrospectively analyzed pts undergoing neoadjuvant chemoradiation (CRT) for locally advanced RCa from January 2012 to July 2021. Pretreatment values of several indices were calculated: neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), lymphocyte to monocyte ratio (LMR), prognostic nutritional index (PNI), systemic immune-inflammation index, systemic inflammation score, systemic inflammatory response index (SIRI), aspartate aminotransferase (AST) to neutrophil ratio index, combination of NLR and LMR, neutrophil to BMI ratio, combination of neutrophil and lymphocyte count, neutrophil-platelet score, lymphocyte × albumin, AST to alanine aminotransferase ratio, and hemo-eosinophil inflammation (HEI) index. Univariate analysis (logrank) on the impact of individual parameters on local control (LC), distant metastases free survival (DMFS), disease free survival (DFS), and overall survival (OS) was performed. A multivariate Cox's analysis of the same endpoints was performed. Was also analyzed the impact of collected parameters on pCR.

Results: We included 105 pts. Univariate analysis is shown in Table 1. At multivariate analysis LMR < 3.78 was a significant predictor of DMFS (HR:0.21; $_{95\%}$CI: 0.06-0.73; p:0.014) and DFS (HR:0.2; $_{95\%}$CI: 0.09-0.86; p:0.026). SIRI ≥ 1.26 was a significant predictor of DMFS (HR:0.18; $_{95\%}$CI: 0.04-0.82; p:0.027) and DFS (HR:0.17; $_{95\%}$CI: 0.04-0.77; p:0.021). At logistic regression male gender (OR 3.78) and increasing PNI (OR

0.87) were significantly predictive of higher pCR rates. NLR ≥ 3.2 was significantly related to worse OS (HR:4.49; $_{95\%}$CI: 1.00-20.19; p:0.050).

Conclusions: Our analysis showed that both LMR and SIRI were independently correlated with DMFS and DFS, and NLR with OS. This information may be useful to develop predictive models able to improve the possibility of personalizing the treatment in this setting. Further studies are underway to evaluate: i) the impact of inflammation markers assessed also after treatment; ii) the possible correlation between inflammation markers and sarcopenia and their predictive role.

Table 1. Univariate analysis on local control, distant metastasis-free survival, disease free survival, and overall survival.



OS: Overall survival; DFS: disease free survival; LC: local control; DMFS: distant metastasis-free survival; BMI: body mass index, cT stage: clinical tumor stage, cN stage: clinical nodal stage; ypT: pathological tumor stage; ypN: pathological nodal stage; TRG: tumor regression grade; EQD2: equivalent dose in 2 Gy fractions; CRT: chemoradiotherapy; NLR: neutrophil-to-lymphocyte ratio; PNI: prognostic nutritional index; LMR: lymphocyte-to-monocyte ratio; NBR: neutrophil-BMI ratio; NLC: combination of neutrophil and lymphocyte count; PLR: platelet-to-lymphocyte ratio; LA: lymphocyte × albumin; HEI Index: Hemo-Eosinophil Inflammation Index; SIRI: systemic inflammatory response index. Statistically significant p-values are shown in bold.

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A PATTERN OF CARE REPORT ON THE MANAGEMENT OF PATIENTS WITH ESOPHAGEAL CANCER - A SURVEY BY THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO) GASTROINTESTINAL TUMORS STUDY GROUP

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Aims: The diagnosis and treatment of esophageal can-

cer (EC) may vary significantly in daily clinical practice, even if international guidelines are available. Based on this background, we conducted a national survey to gain insight into the current management of EC in our country.

Methods: We conducted a pattern of care survey to assess the current management of patients with EC in Italy (40 questions). Twenty-five questionnaires were analyzed.

Results: Most of the respondents work in public and/or university hospitals/IRCCS (92%) in northern Italy (68%). About half (56%) of centers treat 10-20 patients/year (16% > 30 patients/year). Most centers manage patients in a multidisciplinary team (84%). Common examinations for baseline staging include CT scan (100%), esophagogastroduodenoscopy (100%, usually with EUS), and 18FDG-PET/CT scan (92%). The need for jejunostomy/PEG is evaluated on a case-by-case basis in roughly half of centers (44%). For early-stage disease (cT2N0) neoadjuvant radio-chemotherapy (nRCT) is considered instead of upfront surgery in case of high-risk lesions (poorly differentiated, LVI, > 3 cm) by 64% of respondents. For locally advanced disease (cT2-4aN0/+), nRCT followed by surgery is adopted as standard approach in both esophageal squamous cell carcinoma (SCC) (96%) and adenocarcinoma (ADC) (92%). The most frequently prescribed doses are 41.4 Gy/23 fractions (64%) and 50.4-56 Gy/25-28 fractions (40%) in neoadjuvant and definitive setting, respectively. Variability is present in CTV and PTV definition, as well as in the prescription dose (Table 1).

Table 1. Radiotherapy volume definition and prescription dose.

Radiotherapy volume definition for neoadjuvant radio-chemotherapy	
Squamous Cell Carcinoma	
CTV T cranio-caudal expansion from GTV T, cm, median (range)	3 (1-4)
CTV T radial expansion from GTV T, cm, median (range)	1 (0.5-2)
CTV N expansion from GTV N, cm, median (range)	1 (0.5-3)
PTV expansion from CTV, cm, median (range)	0.6 (0-1)
ENI, yes, %	52%
Adenocarcinoma	
CTV T cranio-caudal expansion from GTV T, cm, median (range)	3 (1-5)
CTV T radial expansion from GTV T, cm, median (range)	1 (0.5-2)
CTV N expansion from GTV N, cm, median (range)	1 (0.5-3)
PTV expansion from CTV, cm, median (range)	0.7 (0-1)
ENI, yes, %	52%
Radiotherapy prescription dose for neoadjuvant radio-chemotherapy*	
41.4 Gy/23 fractions	64%
50.4 Gy/28/fractions	32%
Others	28%
Radiotherapy volume definition for definitive radio-chemotherapy	
CTV T cranio-caudal expansion from GTV T, cm, median (range)	3 (1-5)
CTV T radial expansion from GTV T, cm, median (range)	1 (0.5-2)
CTV N expansion from GTV N, cm, median (range)	1 (0.5-3)
PTV expansion from CTV, cm, median (range)	0.7 (0-1)
ENI, yes, %	72%
Boost application, yes, %	88%
- Sequential boost, yes, %	36.4%
- Simultaneous Integrated Boost (SIB), yes, %	63.6%
Boost volume definition for definitive radio-chemotherapy	
CTV T cranio-caudal expansion from GTV T, cm, median (range)	1 (0.5-4)
CTV T radial expansion from GTV T, cm, median (range)	1 (0.3-1.5)
CTV N expansion from GTV N, cm, median (range)	0.9 (0-2)
PTV expansion from CTV, cm, median (range)	0.6 (0-1)
Radiotherapy prescription dose for definitive radio-chemotherapy	
50.4 Gy	32%
50.4-56 Gy	40%
56-60 Gy	16%
>60 Gy	12%

* multiple answers allowed

Most participants use volumetric intensity modulated radiotherapy (76%) and daily volumetric image-guidance (80%). Regarding concurrent chemotherapy, carboplatin-paclitaxel represents the standard of care for ADC and SCC in 80% and 64% of centers, respectively. Induction chemotherapy prior to radio-chemotherapy is considered as an option for extensive locally advanced disease (e.g., cT4b, suspicious extra-regional nodes) by 76% of respondents. The response evaluation is performed within 8 weeks (100%) to the end of nRCT. In case of complete response to nRCT, a watch-and-wait approach with salvage surgery is considered in selected SCC patients in 44% of centers.

Conclusions: Differences were observed among Radiation Oncologists in the management of EC. The results of this survey provide baseline data for future research and to harmonize treatment recommendations for EC patients in Italy.

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A SNAPSHOT ON THE MANAGEMENT OF GASTROESOPHAGEAL JUNCTION CANCER PATIENTS – A SURVEY BY THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO) GASTROINTESTINAL TUMORS STUDY GROUP

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Aims: The treatment of gastroesophageal junction carcinoma (GEJC) may vary significantly in daily clinical practice, as different pre- and peri-operative strategies are included in current international guidelines.

Method: We conducted a pattern of care survey to assess the current management of patients with GEJC in Italy (40 questions). Twenty-five questionnaires were analyzed.

Results: Most of the respondents work in public and/or university hospitals/IRCCS (92%) in northern Italy (68%). About half (56%) of centers treat 10-20 patients/year. Most centers manage patients in a multidisciplinary team (84%). Common examinations for baseline staging include CT scan (100%), esophagogastroduodenoscopy (100%, usually with EUS), and 18FDG-PET/CT scan (92%). The need for jejunostomy/PEG is evaluated on a case-by-case basis in roughly half of cases (44%). For locally advanced disease (cT2-4aN0/+), neoadjuvant radio-chemotherapy (nRCT) followed by surgery is considered standard of care in Siewert I-II lesions (88%), while perioperative chemotherapy represents the treatment of choice in Siewert III lesions (88%). Induction chemotherapy prior to nRCT is considered for extensive locally advanced disease (e.g., cT4b, suspicious extra-regional nodes) by 76% of respondents. The most frequently prescribed dose for nRCT is 41.4 Gy/23 fractions (64%). Variability is present in CTV and PTV definition, prescription dose, and organ motion management (table 1). Most participants use volumetric intensity modulated radiotherapy (76%) and daily volumetric image-guidance (80%). Regarding concurrent chemotherapy, carboplatin-paclitaxel is mostly used (80%). Response evaluation is performed within 8 weeks (100%) to the end of nRCT. In the adjuvant setting, patients underwent upfront surgery are considered for postoperative radiotherapy in addition to chemotherapy in case of non-radical surgery (R1/2) (96%), pT3/4 (36%), pN+ (72%) and/or other risk factors (poorly differentiated, LVI, PNI, age < 50 years) (32%). Conversely, in patients undergoing perioperative chemotherapy and surgery, the addition of postoperative radiotherapy is considered exclusively in case of R1/2 by 60% and not performed by 20% of respondents, respectively.

Conclusions: Differences were observed among centers in the management of GEJC. The results of this survey provide baseline data for future research and to harmonize treatment recommendations for GEJC patients in Italy.

Table 1. Radiotherapy volume definition and prescription dose.

Radiotherapy volume definition for neoadjuvant radio-chemotherapy	
CTV T cranio-caudal expansion from GTV T, cm, median (range)	3 (1-5)
CTV T radial expansion from GTV T, cm, median (range)	1 (0.5-2)
CTV N expansion from GTV N, cm, median (range)	1 (0.5-3)
PTV expansion from CTV, cm, median (range)	0.7 (0-1)
ENI, yes, %	52%
Radiotherapy prescription dose for neoadjuvant radio-chemotherapy*	
41.4 Gy/23 fractions	64%
50.4 Gy/28/fractions	32%
Others	28%
Organ motion management	
Organ motion application, yes, %	84%
- routinely, yes, %	29%
- selected cases, yes, %	71%
Organ motion approach*	
4D-CT/ITV-based	71.4%
4D-CT/gated-based	14.3%
BH	23.8%
Abdominal compression	19%
Others	4.8%

* multiple answers allowed

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A COMPREHENSIVE MULTIVARIATE ANALYSIS OF DIFFERENT SARCOPENIA SCORES IN RECTAL CANCERS UNDERGOING NEOADJUVANT CONCURRENT CHEMORADIATION.

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Aims: Recently, in radiotherapy, interest in sarcopenia (SP) has spread due to its potential prognostic impact. Several studies analyzed the potential of SP evaluation to predict pathological complete response and outcomes in patients with rectal cancer (RCa). However, analyses were performed by using two different SP score systems (Prado et al. 2008; Martin *et al.* 2013) and with only partial consideration of potential confounding factors. Therefore, aim of this study is to compare two SP scoring systems, in an analysis including known prognostic factors, in the setting of neoadjuvant treatment of RCa.

Methods: Patients undergoing neoadjuvant chemoradiation (CRT) for locally advanced RCa from January 2012 to July 2021 were retrospectively found. Pretreatment values of weight, high, body mass index, were obtained and the skeletal muscle index (SMI) were

calculated on a CT-scan at the level of the third lumbar vertebra. Clinical T and N stage, distance from external anal verge, interval between CRT and surgery, age, gender, tumor regression grade by Mandard, pathological tumor stage, pathological nodal stage (ypN), and equivalent dose in 2 Gy/fraction (α/β=10) were also recorded. An univariate analysis (logrank) on local control (LC), distant metastases free survival (DMFS), disease free survival (DFS), overall survival (OS) and a multivariable Cox's analysis on the same endpoints was performed.

Results: We included 105 patients in the study (median age: 63.0 years). The results of univariate analysis are shown in Table 1.

Table 1. Univariate analysis on local control, distant metastasis-free survival, disease free survival, and overall survival.

Variable	Value	Patients N (%)	2-year LC	5-year LC	p-Values	2-year DMFS	5-year DMFS	p-Values	2-year DFS	5-year DFS	p-Values	2-year OS	5-year OS	p-Values
Age (years)	< 55	26 (25)	100	100	0.620	87.3	87.3	0.513	87.3	87.3	0.410	100	95.2	0.310
	55 ≤ age < 70	50 (48)	97.6	97.6		86.8	75.3		84.5	73.2		98	88.6	
	≥70	29 (27)	96.2	96.2		83.6	77.6		83.6	77.6		100	100	
Gender	Male	57 (54.3)	95.7	95.7	0.102	81.3	73.3	0.117	79.1	71.3	0.077	100	92.2	0.462
	Female	48 (45.7)	100	100		91.1	85.8		91.1	85.9		97.7	94.1	
Distance from external anal verge (cm)	0-5	36 (34.3)	93.2	93.2	0.120	87	83.4	0.818	83.5	79.9	0.947	97.1	93.5	0.698
	5.1-10	55 (52.4)	100	100		86.1	76.4		86.1	76.4		100	94.3	
	10.1-15	14 (13.3)	100	100		84.4	84.4		84.4	84.4		100	85.7	
BMI	< 18.5	7 (6.6)	100	100	0.273	100	100	0.472	100	100	0.469	100	100	0.191
	18.5 ≤ BMI <25	47 (44.8)	97.6	97.6		95.8	79.7		85.8	79.7		100	93.3	
	25 ≤ BMI <30	38 (36.2)	100	100		83.1	73		83.1	73		97.4	94.2	
	≥ 30	13 (12.4)	87.5	87.5		87.5	87.5		75	50		100	87.5	
Interval CRT-surgery (days)	< 70	59 (56.2)	98.1	98.1	0.738	92.8	82.4	0.103	90.9	80.8	0.159	100	93.1	0.383
	≥ 70	46 (43.8)	97.4	97.4		76.4	67.9		76.4	76.4		97.8	94.7	
cT stage	2	7 (6.7)	100	100	0.425	85.7	85.7	0.483	85.7	85.7	0.542	100	85.7	0.346
	3	80 (76.2)	98.5	98.5		88.6	79.9		87.1	78.5		98.8	92.8	
	4	18 (17.1)	93.8	93.8		75.6	75.6		75.6	75.6		100	100	
cN stage	0	27 (25.7)	100	100	0.532	95.7	91.1	0.055	95.7	91.1	**0.039**	100	100	0.176
	1	66 (62.9)	96.4	96.4		79.4	72.9		77.6	71.2		98.5	88.5	
	2	12 (11.4)	100	100		100	85.7		100	85.7		100	100	
TRG (Mandard)	1	26 (24.7)	100	100	0.822	96.2	90.8	0.102	96.2	90.8	0.097	100	90.9	**0.049**
	2	17 (16.2)	100	100		100	91.7		100	91.7		100	100	
	3	34 (32.4)	96.7	96.7		87.1	75.3		83.7	72.2		97.1	92.6	
	4	26 (24.8)	95.8	95.8		68.8	68.8		68.8	68.8		100	94.7	
	5	2 (1.9)	100	100		100	50		100	50		100	50	
ypT stage	0	26 (24.7)	100	100	**0.046**	96.2	90.8	**0.050**	96.2	90.8	**0.029**	100	90.9	0.567
	1	9 (8.6)	100	100		100	100		100	100		100	100	
	2	21 (20)	100	100		88.5	82.6		88.5	82.6		100	93.3	
	3	43 (41)	97.3	97.3		76.5	64.8		73.8	55.5		97.7	92	
	4	6 (5.7)	80	80		80	80		80	80		100	100	
ypN stage	0	79 (75.2)	100	100	**0.020**	91.2	87.7	**0.003**	91.2	87.7	**0.001**	98.7	94.5	0.434
	1	19 (18.1)	94.1	94.1		77	53.9		71.1	49.8		100	85.2	
	2	7 (6.7)	85.7	85.7		57.1	57.1		57.1	57.1		100	100	
EQD2 (Gy)	< 50	79 (75)	98.6	98.6	0.278	86.2	79.2	0.939	84.8	77.9	0.845	98.7	93	0.991
	≥ 50	26 (25)	95	95		86	80.2		86	80.2		100	94.1	
Sarcopenia (Prado et al.)	No	69 (66)	98.3	98.3	0.584	88.8	85.1	0.131	87.1	83.4	0.191	98.6	96.8	0.152
	Yes	36 (34)	96.8	96.8		80.7	66.7		80.7	66.7		100	83.7	
Sarcopenia (Martin et al.)	No	67 (64)	98.2	98.2	0.674	91.5	89.4	**0.006**	89.7	87.6	**0.012**	98.5	96.6	0.244
	Yes	38 (36)	97.1	97.1		76.8	61.4		76.8	61.4		100	86.3	

OS: Overall survival; DFS: disease free survival; LC: local control; DMFS: distant metastasis-free survival; BMI: body mass index, cT stage: clinical tumor stage, cN stage: clinical nodal stage; ypT: pathological tumor stage; ypN: pathological nodal stage; TRG: tumor regression grade; EQD2: equivalent dose in 2 Gy fractions; CRT: chemoradiotherapy. Statistically significant p-values are shown in bold.

At multivariable analysis no parameter was significantly correlated to LC or OS. Instead, SP scored with the system by Martin et al. was significantly correlated to worse DMFS (HR: 2.71, 95%CI: 1.04-7.10; p: 0.041). Furthermore, ypN was significantly correlated to DMFS (HR: 5.05, 95%CI: 1.36-18.74; p: 0.015) and DFS (HR: 4.18, 95%CI: 1.60-10.90; p: 0.015).

Conclusions: Our analysis did not show significant correlations with OS of two different SP score systems in RCa treated with preoperative CRT. However, the SP score system by Martin et al. was independently correlated with DMFS. This information may be useful to develop predictive models able to improve the possibility of personalizing the treatment. Further studies are underway to evaluate: i) a new SP score system; ii) the possible correlation between inflammation markers and sarcopenia and the predictive role in this setting of the combination of these emerging parameters.

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PREOPERATIVE INTENSITY-MODULATED RADIOTHERAPY WITH A SIMULTANEOUS INTEGRATED BOOST COMBINED WITH CAPECITABINE IN LOCALLY ADVANCED RECTAL CANCER: LONG-TERM RESULTS OF A MULTICENTRIC STUDY

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Aims: Preoperative radiotherapy (RT) alone or combined with fluoropyrimidine-based chemotherapy (CT) is the standard of care in patients with locally advanced (stage II-III; cT3-T4 N0-2) rectal cancer (LARC). Based on the correlation between RT dose-tumor response and the prognostic role of the pathologic complete response (pCR), multiple studies have evaluated the feasibility, efficacy and toxicity of dose-escalation in the preoperative treatment of LARC. In this pooled analysis, we reported on the long-term results of preoperative RT dose-intensification combined with capecitabine.

Methods: We retrospectively analyzed patients with LARC treated with intensity-modulated radiotherapy (IMRT) and simultaneous integrated boost (SIB) associated with concurrent capecitabine, in ten Italian radiation oncology centers. Acute toxicity and tumor regression grade (TRG) were evaluated according to CTCAE 4.0 scale and Mandard score, respectively. Treatment effectiveness was evaluated in terms of overall survival (OS), disease-free survival (DFS), local recurrence (LC) and distant metastases (DM). A minimum follow-up of two years was requested.

Results: A total of 307 patients was included in this analysis. The median distance anal verge-tumor was 50 mm (range 20-70). Most of patients (77.6%) had a stage III disease, including 33% with N2 subgroup; 42.6% of cases had mesorectal fascia involvement. A dose of 45 Gy was prescribed to the entire mesorectum and pelvic lymph nodes with a median SIB dose of 54 Gy (range 52.5-57.5) to the tumor and corresponding mesorectum. Globally, the treatment was well tolerated; the most common grade 3-4 toxicities were gastrointestinal (5.6%) and haematological (1.9%). Patients underwent surgery after a median time of 82 days (range 71-96) from the end of RT. Thirty percent of cases obtained a pathological complete response (TRG 1). The 2- and 5-year OS were 95.3% and 85.3%, respectively; while the 2- and 5-year DFS were 81.9% and 70%, respectively. LC rate at 2- and 5-year were 5.2% and 11.3%, respectively; while DM rate was 15.4% at 2-year and 23.6% at 5-year.

Conclusions: Preoperative RT dose-intensification concurrent with capecitabine is well tolerated and effective in patients with LARC, especially if they have negative prognostic factors. Although based on a retrospective analysis, these results prompt us to use this approach as RT standard schedule in patients with intermediate and high-risk LARC.

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THE IMPACT OF LYMPHOPENIA ON OUTCOMES IN PATIENTS WITH ESOPHAGEAL OR ESOPHAGEAL GASTRIC JUNCTION CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY PRELIMINARY RESULTS OF A MONO-INSTITUTINAL EXPERIENCE

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Aim: Predictive value of lymphopenia in patients (pts) with esophageal cancer (EC) is unclear, high grade of lymphopenia is associated with worse prognosis. We evaluated the impact of lymphopenia on outcomes in our pts with EC and esophageal gastric junction cancer (EGJC) treated with neoadjuvant chemoradiotherapy.

Methods: from April 2014 to April 2022, 97 pts (F:19; M:78), with histologically proven EC or EGJC were treated according to CROSS study. Median age 63 y (29-80), median KPS 90 (80-100). Fifty-five pts (57%) adenocarcinoma, 41 pts (42%) squamous cell carcinoma and 1 pt (1%) adeno-squamous carcinoma. All pts underwent CT/PET simulation, repeated for restaging. Radiotherapy (RT) consisted in 41.4 Gy/23 fr concomitant to chemotherapy (ChT) with carboplatin and paclitaxel. Acute toxicity was assessed by CTCAE v5.0.

Results: clinical stage was T1: 4 pts, T2: 22 pts, T3: 67 pts, T4: 4 pts, N0: 23 pts, N+: 74 pts. Tumor site was: proximal 6 pts, middle third 22 pts, distal third 41 pts and EGJ 28 pts. Median tumor length was 5 cm (1-15). Tomotherapy was used in 70% of pts and VMAT in 30% of pts. One pt interrupted RT (COVID+). Median number of ChT cycles was 5 (1-6), 70% pts received full ChT dose. The main acute toxicity was lymphopenia in 91/96 pts (95%), in particular 68% had G3-G4 lymphopenia and 27% had G2. Three consecutive pts (3%) had bacterial pneumonia, 1 had aorto-esophageal fistula and underwent early surgery. There is no difference between mean PTV in pts with G0-G2 (843.1 cc) and pts with G3-G4 lymphopenia (852.3 cc) and in term of median tumor length (G0-G2: 5 cm (1-12 cm); G3-G4: 5 cm (1-15)). Median time to restaging was 42 days (14-87), 76/97 pts underwent surgery (21 pts excluded from surgery; PD 8 pts; worsening clinical condition 6 pts; died 1pt; lost 2 pt; cCR 2 pts; not yet operated 2 pts). Post-surgical stage was T0: 16 pts, T1: 12 pts, T2: 16 pts, T3: 31 pts, T4: 1 pt; N0: 48 pts, N+: 28 pts. Mandard TRG was TRG1 16 pts (21%), TRG2 16 pts (21%), TRG3 32pts (42%), TRG4 11 pts (15%), TRG5 1 pt (1%). One-year mortality was 24% (16/66) in pts with G3-G4 lymphopenia vs 19% (6/31) for G0-G2. Two-year mortality was 39.4% (26/66) in pts with G3-G4 vs 32% (10/31) for G0-G2 lymphopenia.

Conclusions: Lymphopenia can predict the prognosis of pts in EC or EGJC. Other predicting factors should be studied to limit the incidence of lymphopenia, in order to assess benefit from checkpoint inhibitors or other lymphocyte-mediated immunotherapies.

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BASAL NUTRITIONAL ASSESSMENT BY SIMULATION-CT SCAN SKELETAL MUSCLE INDEX IN RECTAL CANCER AS A BIOMARKER FOR NEOADJUVANT CHEMORADIOTHERAPY COMPLIANCE AND SURVIVAL

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Aims: Nutritional status has been proven to be an effective prognostic marker in gastrointestinal malignancies. Studies have shown a correlation between skeletal muscle mass (SMM) and nutritional status. The purpose of this study was to investigate the prognostic impact of low SMM before neoadjuvant chemoradiotherapy (nCRT) in patients (pts) affected by locally advanced rectal cancer (LARC) in terms of treatment compliance and overall survival (OS).

Method: Data from LARC pts treated with nCRT at our institution between 2010 and 2020 were retrospectively collected and analyzed. All pts underwent a simulation computed tomography (sCT) scan. Skeletal muscle area (SMA) was obtained from a single slice at the level of the third lumbar vertebra on the sCT. Skeletal muscle index (SMI) was calculated by normalizing SMA by height squared. Sarcopenic obesity was identified in case of obesity (body mass index-BMI≥30) and a low SMI. RT compliance was considered in terms of RT interruption and gastrointestinal (GI) toxicity≥3, according to the Common Terminology Criteria for Adverse Events v5.0. Univariate and multivariate logistic regression analysis was used to identify factors associated with acute toxicity during nCRT. Furthermore, a multivariable Cox regression model was developed, including all variables with $p<0.05$ at univariate analysis, to assess the impact on OS.

Results: A total of 340 LARC pts were enrolled for the final analysis (Table 1). The mean SMI was 50.0 ±9.5, and 121 pts (35.6%) were sarcopenic. The population included 86 obese pts (25.3%), of whom 12.8% had a low SMI (obese sarcopenic pts). A total of 72 pts (21.2%) had temporary treatment interruption due to toxicity; the average number of days of interruption was 8.9. The incidence of acute GI toxicity ≥3 was 24.4%. At univariate and multivariate analysis, SMI was found to be an independent factor of nCRT interruption (OR: 0.95, 95% CI 0.92-0.99; p=0.02). At multivariate Cox regression analysis, both pCR (HR: 0.41, 95% CI 0.21-0.79; p=0.008) and sarcopenic obesity (HR: 4.47, 95% CI 1.87-10.69; p<0.0001) were independent factors for OS.

Conclusions: A low SMI appears to be an economical and easily acquired biomarker to predict nCRT compliance and, in the context of obese pts, OS. This hypothesis-generating study suggests that the SMI of sTC may allow personalization of nutritional support before and during nCRT in LARC pts, improving treatment compliance and survival.

Table 1.

Patients' characteristics	Number (%)
Gender	
Male	207 (60.9)
Female	133 (39.1)
Median age (range)	64 (26-82)
T stage	
2	24 (7.1)
3	206 (60.5)
4	110 (32.4)
N Stage	
0	33 (9.7)
+	307 (90.3)
Mean BMI (kg/m^2)± standard deviation (SD)	26.5 ± 3.8
Obese patients	86 (25.3)
Mean SMI ± SD	50 ± 9.5
Low SMI	121 (35.6)
Sarcopenic obese patients	11 (3.2; 12,8% of obese patients)
Treatment characteristics	**Number (%)**
Median RT dose (Gray) (range)	55 (19.8- 58.5)
Concomitant CT schedule	
Capecitabine/5-FU	146 (42.9)
Capecitabine/5-FU + Oxaliplatin	194 (57.1)
Consolidation CT	62 (18.3)
RT interruption	
Yes	72 (21.2)
No	268 (78.8)
Mean interruption days ± SD	8.9 ± 7.8
Acute GI toxicity	
G1	84 (24.7)
G2	92 (27.1)
G3	72 (21.2)
G4	11 (3.2)

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STEREOTACTIC BODY RADIATION THERAPY IN BORDERLINE RESECTABLE AND LOCALLY ADVANCED PANCREATIC CANCER: LONG-TERM CLINICAL OUTCOME, TOXICITY AND PROGNOSTIC FACTORS

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Aims: The aim of the study was to assess the efficacy and the tolerance of stereotactic body radiation therapy (SBRT) in patients affected by borderline resectable pancreatic cancer (BRPC) and locally advanced pancreatic cancer (LAPC), evaluating long-term clinical outcomes, toxicity profile and prognostic factors.

Method: All patients with BRPC and LAPC were treated with a prescription dose of 45 Gy in 6 fractions using volumetric modulated arc therapy (VMAT) by RapidArc. No patient had nodal and metastatic disease. Primary endpoint was local control (LC), secondary endpoints were distant progression free survival (DPFS), overall survival (OS), toxicity and prognostic factors. We performed an univariate and a multivariate analysis to evaluate a correlation between endpoints and prognostic

factors such as age, tumor diameter, target volumes, time between diagnosis and SBRT, pre-SBRT and post-SBRT CA 19-9 values. Acute and late toxicities were recorded according to CTCAE v5.0.

Results: Between 2010 and 2021, 142 patients with BRPC (9.8%) and LAPC (90.2%) underwent SBRT. Demographic, clinical and treatment characteristics are shown in Table 1. Median follow-up was 10.4 months (2.9 - 81.2 months). Seventy-six patients (53.5%) underwent induction chemotherapy (ChT) and in 42 patients (29.6%) ChT was also administered after SBRT. One-, 2- and 3-year LC rate was 81.9%, 69.1% and 58.5%, respectively. According to RECIST criteria, we observed one patient with complete response (0.7%), 31 partial response cases (22%), 81 patients showed disease stability (57%) and 29 (20.3%) had a local progression. Median DPFS was 6.03 months; 1- and 2-year DPFS rate was 19.9% and 4.5%. Twelve patients (8.4%) were alive at the time of analysis and 7 of them (5%) had no evidence of local and metastatic disease. After SBRT, 4 patients (3%) underwent surgery with negative margins. Median OS was 11.6 months and 1-, 2- and 3-year OS rate was 45.4%, 16.1% and 9.8%, respectively. At univariate analysis, age <70 years (p = 0.037), pre-SBRT ChT (p = 0.004) and post-SBRT ChT (p = 0.019) were significantly associated with OS. We did not observe acute and/or late G3 toxicity.

Conclusions: SBRT has proven to be an effective and safe therapeutic option inside a multimodal approach to improve LC in patients affected by BRPC and LAPC. We observed a better OS when SBRT was sequentially integrated with ChT compared with SBRT alone.

Table 1. Patients' and treatment's characteristics (n=142).

Mean age (range)	71 years (41-91)
Tumor location (number of patients, %)	
- Head	91 (64.1%)
- Uncinate process	23 (16.2%)
- Body	20 (14.1%)
- Tail	3 (2.1%)
- Isthmus	5 (3.5%)
CA19.9 before SBRT	124 (87.3%)
<300 U/mL	79 (63.7%)
>300 U/mL	45 (36.3%)
Not available	18 (12.7%)
Median value (range) [U/mL]	102.75 (0.8-12.000)
CA19.9 after SBRT	
Median value (range) [U/mL]	35 (0.4-8594)
Median diameter (cm, range)	3.7 (1.4-9.3)
Median volume (cc, range)	
CTV	31.6 (2.75-187)
PTV	71.3 (17.6-321)
Chemotherapy before SBRT	
Yes	76 (53.5%)
No	66 (46.5%)
Chemotherapy scheme before SBRT	
- Gemcitabine	7 (9.2%)
- FOLFIRINOX	18 (23.7%)
- Gemcitabine + nab-paclitaxel	17 (22.3%)
- GEMOX	21 (27.6%)
- PEF-G	10 (13.2%)
- Others	3 (4%)
Chemotherapy after SBRT	
Yes	42 (29.6%)
No	100 (70.4%)
Chemotherapy scheme after SBRT	
- Capecitabine-based	5 (12%)
- FOLFIRINOX	6 (14.3%)
- Gemcitabine-based	22 (52.4%)
- Irinotecan	2 (4.7%)
- Others	7 (16.6%)

FOLFIRINOX: folinic acid, 5- fluorouracil, irinotecan, oxaliplatin; GEMOX: gemcitabine, oxaliplatin; PEF-G: cisplatin, epirubicin, 5-fluorouracil, gemcitabine;

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NEW DOSIMETRIC PARAMETERS TO PREDICT ANO-RECTAL TOXICITY DURING RADIOTHERAPY TREATMENT

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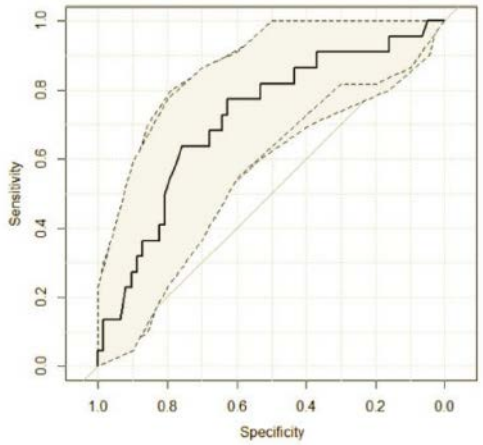
Purpose: Radiotherapy is essential in the treatment of locally advanced rectal cancer. Side effects of radiotherapy in the treatment of rectal cancer have a great effect on quality of life. The aim of this retrospective study is to evaluate the correlation between dosimetric parameters and acute toxicity in rectal cancer patients.



ROC curve of the predictive model elaborated for proctitis with the 95% confidence intervals depicted in dash lines.

Figure 1.

Methods: We analyzed the Dose Volume Histogram parameters for both the target structures and the Organs at risk of 89 patients. A dedicated statistical analysis was performed for all the acute toxicities showing a frequency rate higher than 20%. A linear logistic regression model was elaborated using the variable showing the highest

level of significance at the univariate analysis.

Results: The occurrence of proctitis was significantly correlated with three dosimetric parameters: D98% of low ano-rectum, D98% and Dmean of low ano-rectum wall. A predictive linear logistic regression model reports that the D98% of the wall of the low ano-rectum must be < 38.5 Gy to decrease the rate of proctitis. A general analysis on grade 2 acute toxicity occurrence reported that it was correlated with D98% of low ano rectum.

Conclusions: Two dose constraints were elaborated: D98%<33.5 Gy for low ano rectum to prevent grade 2 acute toxicity and D98%<25 Gy for low ano-rectum wall to prevent proctitis (grade 1 or superior).

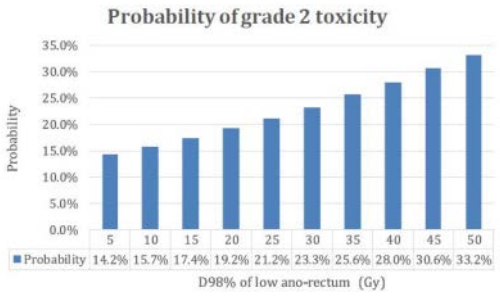


Figure 2.

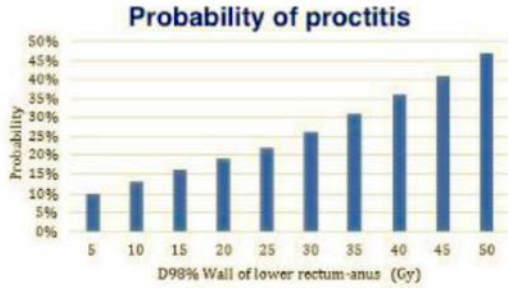


Figure 3.

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HYPOFRACTIONATED RADIOTHERAPY CONCOMITANT TO CAPECITABINE AFTER INDUCTION CHEMOTHERAPY FOR LOCALLY ADVANCED PANCREATIC CANCER

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Aims: We previously showed that moderately hypofractionated radiotherapy (RT), 44.25 Gy in 15 fractions (frs) is feasible after induction chemotherapy with acceptable acute and late toxicity rate and seems to be as effective as standard dose and fractionation (Congress proceeding AIRO 2021, C064). A very high dose (BED=98Gy) were administered at MSKCC in 15 or 25 frs with excellent local control and survival (Reyngold et al, JAMA Oncol 2021;7:735-738), however the best therapeutic window of dose is not well established. We decided to slightly increase the dose of our hypofractionated regimen. Early report on feasibility and acute toxicity is presented.

Methods: Patients (pts) with histologically confirmed locally advanced pancreatic cancer (LAPC) were treated with induction chemotherapy (ChT) and subsequently restaged. Pts with no distant progression and still deemed not resectable were candidate for radiochemotherapy (RCT). Pts underwent simulation contrast-enhanced CT and FDG-PET/CT. CTV included the GTV with a margin of 1 cm, mesenteric axis, celiac axis (only for tumors of body and tail). PTV1 was defined as CTV expanded of 1-1-1.5 cm. ITV was defined as GTV with margins of 0.5-0.5-1-0 cm. BTV was merged with ITV. An isotropic margin of 0.5 cm was added to ITV/BTV to create PTV2. A dose of 37.5 Gy and 50 Gy in 15 frs was prescribed to PTV1 and PTV2, respectively. A dose of 44.25 Gy was prescribed to the overlap between PTV2 and PRVs created expanding stomach and duodenum of 0.5 cm. Constraints for stomach were: V40<18cc, V30<23cc; constraints for duodenum were: V45<1cc, V40<15cc, V30<35cc. Concomitant chemotherapy was capecitabine, 1250 mg/day.

Results: Fourteen pts were treated from 5/2021 to 4/2022. Median follow up was 8.1 months. All pts concluded RCT without interruption. Acute toxicity. G1- G2 nausea/vomiting: 9 pts (64%), G1-G2 anorexia: 4 pts (28.5%); G1 epigastric pain 4 pts (28.5%); G1 fatigue 3 pts (21%); G1 diarrhea 1 pt (7%), G1 weight loss 1 pt (7%). Hematological toxicity. G2 lymphopenia: 3 pts (21%); G3 lymphopenia: 2 pts (14%); G1 neutropenia: 1 pt (7%); G1 thrombocytopenia: 1pt (7%). Late toxicity. G2 gastritis and ulcerations in 1 pt (7%) who had portal gastropathy due to hilar hepatic progression and portal thrombosis. Median follow up is too early for outcome data.

Conclusions: Our regimen of hypofractionated RT concomitant to capecitabine after induction ChT seems to be feasible with an acceptable toxicity rate. Accrual is ongoing.

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CHEMORADIATION IN PRIMARY OR RECURRENT UNRESECTABLE BILIARY CANCER: A SYSTEMATIC REVIEW AND METANALYSIS

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Aim: Biliary tract cancers (BTC) are rare and aggressive neoplasms. Based on international guidelines, the management of locally advanced or unresectable disease is based on chemotherapy (CHT). Chemoradiation (CRT) may represent an alternative treatment in this setting. Aim of this study is to review the current knowledge on concurrent CRT for primary or recurrent unresectable BTC.

Method: Papers were searched on Pubmed, Scopus, and Cochraine Library. Prospective or retrospective trials reporting outcomes on concurrent CRT for unresectable, non-metastatic, primary or recurrent BTC were included. Only English-written papers, published from January 2010 to January-2022 were considered.

Results: Sixteen papers were considered in the analysis, with a total of 1932 patients included. Ten papers focused on primary unresectable BTC, two papers treated isolated local recurrences, four papers considered both situations. Ten papers (62.5%) included a mixed population with diagnosis of intrahepatic, extrahepatic, hilar cholangiocarcinoma, and gallbladder cancer, mostly with advanced stage of disease (median percentage of T3-4 was 69.8%). A median dose of 54.0 Gy (range 45.0-72.6 Gy) in conventional fractionation was delivered. Concurrent CHT was mainly based on 5-Fluorouracil or Gemcitabine schedules. Median Overall survival (OS) and Progression free Survival were 13.5 and 8.9 months, respectively. One- and 2-year OS median rates were 64.3% and 32.0%, respectively. Grade ≥3 acute gastrointestinal toxicity ranged from 5.6 to 22.2 % (median: 10.9%) while grade ≥3 acute haematological toxicity ranged from 1.6 to 50.0% (median: 21.7%). Four papers compared OS after CRT versus CHT with hazard ratio (HR) values between 0.58 and 0.80 in favour of CRT. A meta-analysis was performed confirming the improved OS after CRT (pooled HR: 0.70) (Figure 1).

Conclusions: CRT seems an effective alternative to standard CHT. All papers reporting a comparison between CRT and CHT showed a significant advantage after CRT in terms of OS. Therefore, randomized comparative trials are needed in this setting.

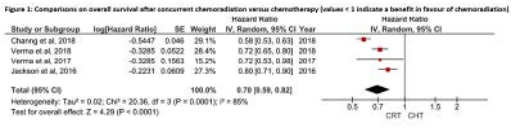

Figure 1.

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DOES THE CT-PET POST-NEOADJUVANT CHEMO-RADIOTHERAPY PREDICT THE PATHOLOGICAL RESPONSE IN ESOPHAGEAL CANCER? – MONOINSTITUTIONAL EXPERIENCE

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Background: The role of CT-PET in predicting pathological response after neoadjuvant chemoradiotherapy (nCRT) in esophageal cancer (EC) is unclear. The use of CT-PET nowadays is not the standard for treatment planning but can help to define the therapeutic decision detecting distant metastasis at the diagnosis. Predicting pCR before surgery may help selecting patients and choose the best treatment strategy.

Aim: to assess the role of CT-PET post nCRT in predicting pathological response (pR) in esophageal (EC) or esophageal gastric junction cancer (EGJC).

Methods: from April 2014 to June 2022, 97 patients (pts) (F:19; M:78), with histologically proven EC or EGJC were treated according to CROSS study in our Institute. Median age at diagnosis 63 years (29-80), median KPS 90 (80-100). Fifty-five pts (57%) had adenocarcinoma (AC), 41 pts (42%) had squamous cell carcinoma (SCC) and 1 pt (1%) had adeno-squamous carcinoma. Radiotherapy (RT) consisted in 41.4 Gy/23 fractions, concomitant to chemotherapy with carboplatin and paclitaxel. All pts underwent CT-PET simulation, repeated for restaging. CTV was defined as GTV + BTV (T + N) plus 3 cm craniocaudally and 1 cm in the other directions.

PTV was defined as CTV plus 1 cm in all directions. Metabolic response (mR) after nCRT and Mandard tumor regression grade (TRG) based on pathological histological specimens were investigated.

Results: Seventy-six pts out of 97 were evaluable for this analysis (21 pts were excluded from surgery: PD 8 pts; worsening clinical condition 6 pts; Died 1pt; Lost 2 pts; cCR 2 pts; waiting for surgery 1 pt; still in treatment 1 pt). Median time to restaging was 43 days (14-87). Twenty-six pts had mCR, 42 pts had mPR, 4 pts had mSD, and 4 pts had mPD. TRG was TRG1 16 pts (21%), TRG2 16 pts (21%), TRG3 32 pts (42%), TRG4 11 pts (15%), and TRG5 1 pt (1%). Among the 26 patients with mCR, just the 19% of the population had pCR (TRG1); PET was false negative in 81% of patients (21/26) with residual cancer cells (TRG2 to TRG5). Fifty pts (66%) did not present complete response at the PET scans; despite this evidence, PET showed false positive in 22% of the pts (11/50).

Conclusions: In our experience, PET scans does not seem to predict the pathological response, due to the high rate of false negative; it can be indicated as staging exam to choose the best clinical therapeutic option. According to our preliminary data, further analyses are needed to develop new treatment strategies.

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INTENSITY-MODULATED RADIOTHERAPY (IMRT) IN THE TREATMENT OF ANAL CANCER: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: To investigate the toxicity and response in patients with anal squamous cell carcinoma treated by IMRT with a simultaneous integrated boost (SIB)and concurrent chemotherapy (CT).

Methods: From February 2009 to June 2021, we analyzed consecutive patients with a minimum of 1 year-follow up. The most common CT regimen was mitomycin and 5-fluorouracil or mitomycin and capecitabine. IMRT was delivered by helical tomotherapy. We collected data about response and local/distance progression until last follow up. Finally we reported acute and late toxicities according to CTCAE v5.0 classification.

Results: Clinical data of 129 patients (M:31, F: 98) were analyzed. Median age of population was 65.4 years (range: 32-89). 7 patients were HIV positive (5.4%). In 10 pts SCC was localized at anal margin, while 119 had a anal canal SCC. The stage of disease was: stage I in 15 patients (11.6%), stage II in 37 patients (28.7%), stage IIIA in 32 patients (24.8%), stage IIIB in 45 patients (34.9%). IMRT was delivered by a moderately accelerated RT fractionation schedule with a dose of 50-55 Gy and 40-45 Gy in 25-28 fractions to PTV 1-2, respectively. At 6 months from end of RT we evaluated definitive response to treatment: 100/129 pts (77.5%) achieved RC, 23/129 pts (17.8%) had PD (local or systemic), 6 pts (4.6%) were lost at follow up. Of 129 pts, 13 (10.1%) received colostomy due to persistence or local recurrence. Toxicities were represented in population as follows: acute G3 skin toxicity were detected in 42/129 (32.5%) patients, acute G3 GI toxicity in 4/129 (3.1%) patients, acute G3 pain in 20/129 (15.5%) patients; no severe late toxicities were detected. At last follow up 23/129 (17.8%) patients were deceased, of these 11/23 (47.8 %) due to anal cancer, 10/23 (43.4%) due to cancer non related causes and 2 for unknown causes.

Conclusions: In our experience, intensified SIB-IMRT with chemotherapy is very feasible in clinical practice, with excellent results in terms of local control and tolerance.

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RADIOTHERAPY TREATMENT WITH STEREOTACTIC BODY RADIOTHERAPY (SBRT) OF LIVER LESIONS WITH POSITIONING OF HEPATIC FIDUCIAL MARKERS: OUR EXPERIENCE

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Purpose: To describe the technique and to evaluate the safety of fiducial markers implantation for the stereotactic body radiotherapy treatment of liver lesions, and to evaluate the response to radiation.

Materials and Methods: Between January 2020 and December 2020, 10 patients were retrospectively identified (6 men and 4 women; average age 72 years) who underwent stereotactic body radiation treatment at the liver level, performed after placing dedicated fiducial markers. The prescription dose at the GTV was 40 Gy / 5fr. The implantation of the markers was performed percutaneously both under ultrasound guidance (9/10 patients) and under CT guidance (1/10 patients); the markers were placed in or near of the target lesions. The GTV was delineated on fusion of images between CT with MDC and CT of simulation with the help of the dedicated radiologist, an ITV was assessed, following the movement of the fiducial markers, and a PTV was defined by adding 5 mm to the ITV. For the evaluation of post-procedural complications (bleeding, dislocation) both clinical-laboratory parameters (CBC, BP, FC) and follow-up imaging by CT were considered. The treatment plan took into account the OaR literature contraints. A

plan was carried out with VMAT / IGRT cone beam CT daily.

Results: 20 paired fiducial markers were implanted in patients suffering from both primary liver injury (4 HCC) and secondary liver injury (1 case of clear cell renal cell carcinoma metastasis, 1 case of neuro-endocrine tumor metastasis, 4 cases of gastrointestinal tract carcinoma metastases). The procedures were performed under local anesthesia by the same radiologist. In 1 case (1/10) there was a post-procedural, while in another case (1/10) a marker was dislocated, which however did not affect the execution of the stereotactic body radiation treatment. All liver lesions treated are in radiological response at the first follow-up, we did not find any radiotherapy dose acute side effects.

Conclusion: Percutaneous implantation of hepatic fiducial markers for the planning of stereotactic body radiation treatment was found to be a safe, effective and necessary procedure to be able to perform IGRT with daily cone beam CT.

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INOPERABLE BILIARY TRACT CANCER: EXPERIENCE OF COMBINED HYPOFRACTIONATED RADIO-CHEMOTHERAPY

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Aims: Biliary tract cancers (BTCs) are the second most common hepatic malignancy after hepatocellular carcinomas, characterized by aggressive nature and fatal prognosis. Generally, surgical resection represents the only potentially curative treatment for these tumours but, since 50% of patients are diagnosed in advanced stage with unresectable disease, both chemotherapy and radiotherapy can play an important role. Our aim is to evaluate safety and tolerability of combined hypofractionated radio-chemotherapy approach and the outcomes in terms of local control (LC) of disease for patients affected by inoperable BTC.

Method: Basing on literature data, which shows that RT improves cancer specific survival in inoperable patients and dose escalation led to higher LC rates, from 2018 to 2022 at University of Catania, 21 patients with unresectable BTC have been enrolled (Table 1) to receive hypofractionated photon radiation therapy (HF-RT) and chemotherapy. The protocols used for induction, concomitant radiotherapy and adjuvant chemotherapy were Gemcitabine-Oxaliplatin (19.04%), Cisplatin-Gemcitabine (28.57%) Fluorouracil-Oxaliplatin (23.80%), De Gramont (14.28%), and Capecitabine (14.28%). All patient performed HR-RT with the following schedules: 400-2400 cGy (14.28%), 300-3000 cGy (28.57%), 250-5000 cGy (57.14%), all delivered by IMRT or 3D-CRT (Table 2). To evaluate the local control of disease and toxicities, all patients have been radiologically evaluated both before and after 6 weeks from the end of RT treatment and clinically evaluated during the entire course of treatment.

Results: According to CTCAE v4.0, during CT-RT treatment course, the most performed adverse effects have been G1-G2 cutaneous toxicities (38.11%), G1-2 G.E. and haematological toxicities (33.33% and 28.57% respectively) and G3 hematological toxicities (14.28%), only two patients performed severe haemoglobin and platelet decrement needing transfusion. Patients did not experience liver failure, biliary obstruction or cholangitis during RT. After CT-RT all patients underwent MRI restaging showing a rate of local control of disease of 76%.

Conclusions: Even if further studies are needed to decide the best radiotherapy schedules, it can be concluded that hypofractionated radiotherapy with concurrent chemotherapy, in patients with inoperable BTCs, is well tolerated, not related to elevate rates of severe toxicity, and it' associated to best rates of LC of disease.

Tables 1 and 2.

Table 1

Characteristics		Percentage
Sex	Males	85.71%
	Females	14.28%
Age	55-64 y.o.	28.57%
	65-74 y.o.	28.57%
	>75 y.o.	42.85%
Comorbidities	None	14.28%
	Diabetes	33.33%
	Hypertension	52.38%
	Hypercholesterolemia	19.04%
Onset symptoms	Obstructive jaundice	85.71%
	Abdominal pain	28.57%
Localization	Intrahepatic cholangiocarcinoma (iCCA)	14.28%
	Perductal cholangiocarcinoma (pCCA)	28.57%
	Extrahepatic cholangiocarcinoma (eCCA)	38.11%
	Gallbladder cancer	19.04%
Stage	T2 any N	14.28%
	T3 any N	57.14%
	T4 any N	28.57%

Table 2

Treatment		Percentage
Radiotherapy schedules	250-5000 cGy	57.14%
	300-3000 cGy	28.57%
	400-2400 cGy	14.28%
Chemotherapy schemes	Cisplatin-Gemcitabine	28.57%
	Gemcitabine-Oxaliplatin	19.04%
	Folfox	23.80%
	Capecitabine	14.28%
	De Gramont	14.28%

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ANALYSES OF THE LOCAL CONTROL OF LUNG METASTASES FROM COLON-RECTAL CANCER AFTER STEREOTACTIC BODY RADIATION THERAPY: A MONOCENTRIC EXPERIENCE

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Aims: The lungs are the second most common site of distant metastases from colon-rectal cancer (CRC). According to data, 10%-15% of patients with CRC develop lung metastases during the course of the disease. Stereotactic body radiation therapy (SBRT) is a non-invasive therapeutic option for these patients. The aim of this retrospective study is to evaluate the local control of SBRT in patients with lung metastasis from CRC.

Method: Between december 2016 and december 2020, a total of 31 patients (median age 64 years, M:F 1,8:1) presenting with 50 metastases (26 located in upper or medium lobe and 24 in inferior lobe) from colon-rectal cancer were submitted to SBRT at Department of Radiation Oncology, Pisa University, Pisa, Italy. The RT treatment was performed with True Beam LINAC VARIAN System with VMAT technique, using 6MV-FFF photons. We utilized 4D-CT software to determinate the average tumor motion during respiratory cycle (ITV), in case of excessive motion of the nodule breath hold technique, abdominal compression or respiratory gating system was used. Planning tumor volume was obtained by adding to ITV an isotropic margin of 3-5 mm in all directions. All patients received a treatment with a BED10 > 75 Gy; 33 metastases were treated in one fraction of 24-30 Gy, 12 metastases in 3 fractions of 12-15 Gy and 5 metastases in 5 fractions of 10 Gy. In this analysis we evaluated results in terms of local control (LC), defined as absence of local progression at the subsequent CT scan and/or PET.

Results: After a mean follow-up of 30,3 months (range 4-60 months), 24 metastases (48%) were in local progression. The mean time of progression was 10,3 months. 26 metastases were controlled after SBRT for a mean time of 24,8 months. Metastases located not in the lower lung lobe showed higher LC.

Conclusions: The LC rate of this study was relatively low, as expected from previous findings. Higher BED10 tended to achieve higher LC but was not significant because of the effects of other factors. Patients with metastases located in the upper or middle lung lobe are good candidates for local therapy and possibly better candidates for SBRT.

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COULD BE CLINICAL RESPONSE AT 6 MONTH A PREDICTIVE RESPONSE OF DISEASE-FREE SURVIVAL IN ANAL CANCER? A MONOCENTRIC RETROSPECTIVE STUDY

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Aims: To evaluate efficacy and tolerance of curative radiotherapy (RT) concomitant chemotherapy (CHT) in patients (pts) with anal cancer, in terms of acute and early late toxicity, clinical response and survival outcomes.

Methods: thirty-three pts affected by anal tumour were treated from 2012 to 2021, including 75% (25 pts) with a diagnosis of squamous cell carcinoma and 25% (8 pts) with other histological type, with stage I-IIIC. Twenty-nine pts underwent Intensity Modulated Radiotherapy (IMRT), while 4 pts Volumetric Modulated Arc Therapy (VMAT) technique, with a total dose of 55Gy/25 fractions (fr) to the tumor and to positive lymph-nodes and 45Gy/25 fr to pelvis and inguinal stations; in 88% (29 pts) was administered CHT concurrent. Toxicity assessment has been considered in acute and in early-late (up to 12 months post RT completion) for gastrointestinal (GI), genitourinary (GU), cutaneous (CU) and haematological (HT) districts, according to Radiation Therapy Oncology Group (RTOG) scoring system. Clinical response at 6 months was assessed with pelvic MRI or anoscopy for local response and TCTB for distant diseases. Survival outcomes were calculated through Kaplan-Meier curves.

Results: Acute CU G1 toxicity was recorded in 9 pts (27%), G2 in 12 pts (36%), G3 in 4 pts (12%). Acute GI G1 toxicity was registered in 13 pts (39.3%), G2 in 12 pts (36.3%), G3 and G4 in 1 (3%) and 1 (3%) pt respectively. Acute GU G1 toxicity was recorded in 11 pts (33.3%), G2 in 7 pts (21.2%). Acute HT G1-G2 toxicity in 3 (9%) and 5 (15%) pts respectively. Regarding early-late toxicity: CU G1 toxicity was observed in 1 pts (3%) and G2 in 1 pt (3%), GI G1 toxicity was recorded in 16 pts (48%), G2 in 3 pts (9%) and G4 in 1 pt (3%). GU G1 toxicity was observed in 5 pts (15%) and G2 in 2 pts (6%). No early-late HT toxicity was reported. Median survival was 59.7 months. At 2- and 5-years survival probability were as follows: overall survival (OS) 84.2% and 75%, progression-free survival (PFS) 74% in both, local recurrence-free survival (LRFS) 76% in both, metastasis-free survival (MFS) 82% in both respectively. Twenty-nine pts had complete clinical response at 6 month and 83% was disease free survival at 5 years.

Conclusions: RT-CHT combined showed to be effective and safe in this population and low toxicities profile. A statistically significant data (Pvalue <0.005), patients

who presented a clinical complete response at six months had a good response in terms of outcomes.

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VMAT FOR NEOADJUVANT RADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER IN A DOSE-ESCALATION PROTOCOL AND SIMULTANEOUS INTEGRATED BOOST (SIB) APPROACH: THE EXPERIENCE OF OUR INSTITUTION

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Aims: To report the feasibility of volumetric modulated arc therapy (VMAT) for neoadjuvant radiotherapy in locally advanced rectal cancer in a dose-escalation protocol and simultaneous integrated boost (SIB) approach. Moreover, the VMAT technique was compared with three-dimensional conformal radiotherapy (3D-CRT) and fixed-field intensity modulated radiotherapy (IMRT), in terms of target coverage and irradiation of organs at risk.

Methods: Eighteen patients with locally advanced rectal cancer were treated with the SIB-VMAT technique. The VMAT plans were compared with 3D-CRT and IMRT techniques in terms of several clinically dosimetric parameters. The number of monitor units and the delivery time were analysed to score the treatment efficiency. All plans were verified in a dedicated solid water phantom using a two-dimensional array of ionisation chambers.

Results: All techniques meet the prescription goal for planning target volume coverage, with VMAT showing the highest level of conformality. VMAT is associated with 40, 53 and 58% reduction in the percentage of volume of small bowel irradiated to 30, 40 and 50 Gy, compared with 3D-CRT. No significant differences were found with respect to SIB-IMRT. VMAT plans showed a significant reduction of monitor units by nearly 20% with respect to IMRT and reduced treatment time from 14 to 5 min for a single fraction.

Conclusions: SIB-VMAT plans can be planned and carried out with high quality and efficiency for rectal cancer, providing similar sparing of organs at risk to SIB-IMRT and resulting in the most efficient treatment option. SIB-VMAT is currently our standard approach for radiotherapy of locally advanced rectal cancer.

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NEOADJUVANT CHEMOTHERAPY AND RADIOTHERPY FOR LOCALLY ADVANCED RECTAL CANCER. OUR EXPERIENC

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Aims: To evaluate feasibility, tolerance and impact on local control in neoadjuvant chemotherapy and radiotherapy for locally advanced rectal cancer.

Methods: From January 2011 to December 2021, 250 Patients (pts) affected by locally advanced rectal cancer were treated with Neoadjuvant Chemotherapy (capecitabine) followed by radical surgery in our center. All patients had rectal adenocarcinomas, 155 G2 and 95 G3 at pretreatment biopsy. All patients had endoscopy and RM. The majority of patients had also an Endoscopic Ultrasound. At staging 64 patients had T3N0, 85 T3N1, 55 T3N2 and 46 T4aN1. All patients received 50.4 Gy in 28 fraction on whole pelvis, 1,8 GY for fraction. All patients had radical surgery after a median of 55 days (range 50– 60 days). 191 patients had radical anterior rectal resection, 59 pts a “Miles” surgery.

Results: After neoadjuvant treatment 192 pts had G0-1 rectal toxicity, 56 pts G2. In 2 cases treatment was interrupted. In one case per G3 local toxicity in a frail patient, In one case we founded lung progression during treatment. No genitourinary toxicity was recorded. At surgery 75 pts had a T0N0 (30%), 80 T1N0 (32%) 65 T2N0 (26%), 30 patient. T2N1 (12%). 234/250 (94%) patients had a complete response on nodal site initially N+. During follow up one patient ad a gastric cancer (primary, total gastrectomy, NED after a total of 16 month). Four patients T3N1 had a T1N0 at surgery but a local recurrence after a median 14 month. The patient with lung progression during treatment had also liver metastasis 6 month after initial treatment, and died after 17 month. No patients had post treatment permanent toxicity.

Conclusions: Our data suggests the feasibility of the treatment, because it results in a nonaggressive management, with good results in desease local control.

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CHEMORADIATION THERAPY AS DEFINITIVE TREATMENT OF ESOPHAGEAL CANCER: STATE OF THE ART REVIEW

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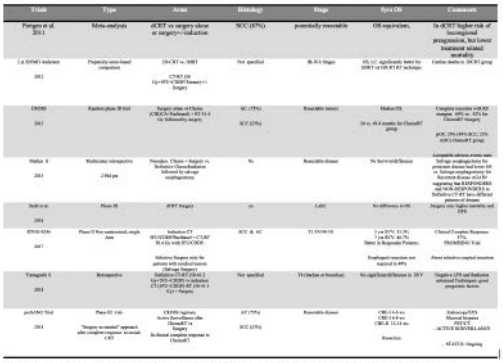
Aims: Esophageal cancer (EC) is an aggressive tumor, with a poor prognosis and an overall 5-year survival rate of 15-25%. Main histologic subtypes of EC are squamous cell carcinoma (SCC) and adenocarcinoma (AC), with different geographic incidence. Although esophagectomy remains the mainstay of treatment for EC, only 25% results in early-stage resectable disease. For locally advanced EC patients, a multimodality therapy integrating neoadjuvant and/or adjuvant chemotherapy and radiation therapy (RT) with surgery is widely accepted based on high-level evidence. Moreover, esophagectomy is an invasive treatment, with substantial perioperative morbidity and postoperative sequelae with impaired patients' quality of life.

Method: A narrative review was performed on Pubmed using "Chemoradiation Therapy" OR "Definitive Chemoradiotherapy" AND "Esophageal Cancer". Selected papers were in English, with a study design of systematic review, meta-analysis and clinical trials.

Table 1.

studies comparing definitive Radio-chemotherapy to surgery, Radiotherapy techniques, and watch and wait approach



dCRT: definitive chemoradiotherapy, SCC: squamocellular cancer, OS: overall survival, RD-CRT: 3dimensional chemoradiotherapy, IMRT: intensity modulated radiotherapy, LC: local control, AC adenocarcinoma, pCR: complete pathological response, ns: not specified, LaSC: locally advanced esophageal cancer, DFS: disease free survival, LFN: lymphonodes, CRE: clinical response evaluation, PET TC: Positron emission tomography and Computed Tomography.

Results: For patients who decline or are medically unfit for surgery, definitive chemoradiotherapy (dCRT) is an alternative approach. It's the standard of care for cervical EC, extending from the hypopharynx to the sternal notch. Most of studies combined SCC and AC, even if their biological behavior and outcomes are different. AC is less responsive to chemoradiation, with high tendency to metastasize. For this reason, multimodality approach with surgery after chemoradiation is the standard of care. For locally advanced SCC, effect of adding surgery to chemoradiation has shown no difference in overall survival, although a substantial improvement in local control was assessed in the surgical arms. After RCT a complete pathological response is achieved up to 50% of SCC patients and 25% of AC, looking for organ preservation (Table 1).

Conclusions: dCRT shifted paradigm of curative treatment in EC. Particularly, for not resectable disease, dCRT allowed a better prognosis, changing from palliative to curative intent. For SCC patients, mostly for cervical location, dCRT is the standard of care. For SCC achieving a pCR after dCRT, a close surveillance could be a good option. Salvage esophagectomy for residual of disease after dCRT should be taken in account, with Disease Free Survival and Overall Survival compared to trimodality approach.

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ROLE OF 18F-FDG-PET IN PREDICTING TUMOR RESPONSE AND OUTCOMES IN RECTAL CANCER TREATED WITH PREOPERATIVE RADIOTHERAPY. A REVIEW OF SYSTEMATIC REVIEWS AND META-ANALYSES

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Aims: The ability to predict response and outcome in rectal cancer patients undergoing neoadjuvant therapies would have the potential to allow for treatment adaptation and personalization. Several studies tested 18F-FDG-PET for this purpose and the results of these analyses have been included in a series of systematic reviews and meta-analyses. The purpose of this review is to summarize and analyze these latest reports.

Methods: A literature search was performed in PubMed, Scopus and Cochrane library. After the removal of the duplicate papers, 271 reports were screened and of these 263 were excluded. Finally, 8 papers were included

in this review and the following elements were extracted independently by two authors: type of analysis (systematic review or meta-analysis), number and design of included studies, timing of PET, evaluated PET parameters, results of the analysis, and authors' *Conclusions:*

Results: The results of the review are summarized in Table 1. All studies recorded a high accuracy of early (interim) 18F-FDG-PET in predicting tumor response with pooled sensitivity and specificity values greater than 80% and higher compared to those of morphological imaging, although with less precise results for the prediction of complete pathological response. The PET-related parameter with the greatest predictive power of tumor response is the "response index", while the analyzed studies have uniformly reported a significant correlation between 18F-FDG-PET results and overall survival. Conversely, a systematic review showed a significant correlation between 18f-FDG-PET response with disease-free survival while a meta-analysis reported the lack of such a correlation.

Table 1. Systematic reviews and meta-analyses.

Author/ year	Type of study	No & design of studies	RT/CRT	PET timing	Evaluated PET parameters	Results	Conclusions
Ferrari M. et all 2017	SR	12 PROS; 1 RETR	CRT	18F FDG PET/CT interim performed at 1 (3/13 studies), 2 (8/13 studies), 3 (1/13 study) w after neoadjuvant CRT.	SUVmax, ΔSUVmax, SUV mean and ΔSUVmax in 2/13; SUVmax and ΔSUVmax in 6/13 studies. TLG in 2/13 studies, only SUV max in 1 study, tumor diameter in 2/13 studies.	all studies suggest a possible role of interim PET/CT in the distinction of non-metabolic responders from responders	PET could in future identify non-responder patients and avoid ineffective therapy and to shift to potentially more effective alternatives including anticipated radical surgery
Maffione AM et al 2015	SR & MA	17 PROS; 17 RETR; MA on 2934 studies	CRT	Pooled time to PET during and after CRT was 1.5 and 6.1 w, respectively.	RI in 50% of the global cohort and in 88% of all interim studies; SUVmax post CRT and VRA, peack cand in 18% of studies	FDG-PET/CT had good pooled accuracy, both in the global cohort of 1526 patients (pooled sensitivity, 73%; pooled specificity, 77%; pooled AUC, 0.83) and for subgroups. There is high pooled accuracy for early PET re-staging, performed between 1 and 2 weeks after the beginning of CRT (pooled sensitivity, 84%; pooled specificity, 81%; pooled AUC, 0.89). Pooled cutoff values for RI and SUVmax post are 69% and 4.4, respectively	It is not possible to predict optimal timing for PET during and after chemoradiotherapy for locally advanced rectal cancer.
Joye I et al. 2014	SR	20 PROS; 4 RETR	CRT	18F FDG-PET/CT prior to the start of CRT (in 13/24 studies), after 15-17 fractions, or 4 days, or 2 w of CRT (in 3/24 studies), after the end of CRT (in 2/24 studies, with intervals CRT- PET ranging from 1-12 w)	SUVmean pre CRT, SUVmax pre CRT in 13/24 studies, SUVmean during CRT, SUVmax during CRT in 3/24 studies, SUVmean post CRT, SUVmax post CRT in 14/24 studies, ΔSUVmax, RI SUVmean, RI SUVmax, TLG and MTV (in 3/24 articles), VRS (in 11/24 studies)	Quantitative and qualitative 18F-FDG PET/CT measurements are equally effective in the assessment of pCR after CRT. The major strength of 18F-FDG-PET/CT lies in the identification of non-responders who are not candidates for organ preservation. However, 18F-FDG PET/CT is not accurate enough to safely select patients for organ-sparing strategies.	future research must focus on the integration of functional imaging with clinical data and molecular biomarkers
Li C et al 2014	MA	17 PROS; 14 RETR	CRT	18F FDG-PET performed pre CRT in 5/9 studies, during CRT in 2/9, after CRT in 4/9; 18F FDG PET/CT performed pre/CRT in 23/25, during CRT in 7/25, after CRT in 18/25 studies.	V/K in 8/31 studies; RI in 28/31 studies, SUV max post CRT in 13/31 studies. 67% in 3/31 studies.	18F-FDG PET could be a potentially powerful non-invasive tool for predicting pathological response, the related parameters RI and SUVmax-post may be more suitable for the prediction of TRG than pCR.	the optimum post treatment 18F-FDG PET scan could be carried out during CRT.
Maffione AM et al 2014	SR	10 PROS	CRT	Mean time to perform PET during CRT: 1.8Gy	SUV max at baseline, SUV max at interim and RI in all studies; moreover, in 6/10 studies ΔSUVmean and in 2/10 studies ΔTLG values	PET has high accuracy in early prediction response during preoperative CRT, increased with the use of RI as parameter	an early assessment of non-responder patients allows modification of the subsequent
							strategy especially the timing and the type of surgical approach
Koug B et al 2013	SR & MA	5 PROS	CRT	18F-FDG PET/CT or 18F-FDG PET before and after (2-6 w) CRT	SUVmax pre CRT, SUVmax post CRT (ΔSUV)	18FDG-PET is a significant univariate predictor of overall survival, but not for time to recurrence	/
de Geus-Oei LF et al 2009	SR	16 PROS	CRT and 1 RETR	Timing PET after therapy: 2-3 w (11/16); RT (5/16)	-ΔSUVmax in 10/16 studies; ΔMRglu and -ΔCT-/-MTV volume in 11/16 studies each; visual response score in 6/16 studies. -RTU in 3/16 studies. SUV cutoff level after radiotherapy 2.2 and SUV ratio in 2/16 studies. -ΔSUV mean >62% (after 12 days) in 1/16	18F-FDG PET after neoadjuvant treatment is important for the preoperative selection and for an individually tailored surgical approach due to better correlation with pathology than morphologic imaging modalities	being 18F-FDG PET able to predict the final outcome, it may be used to guide adjuvant chemotherapy for rectal cancer after optimal neoadjuvant and local treatments
Vliena D. et al2008	SR	16 PROS; 2 RETR	CRT (16/18); RT (2/18)	18F-FDG PET before start of (C)RT, and at different intervals after the end of (C) RT (from 12 days up to 7w)	SUVmax (11/16); SUVmean (1/16); SUVmean ratio (1/16); ΔSUVmax (6/16); ΔSUVmean (3/16); VRS (6/16); ΔTLG (2/16)	Histological T-stage decrease correlated to -ΔSUVmax in responders vs non-responders (-3.5 vs -1.6; p 0.05) in 1/16; -ΔSUVmax>36% to identify responders vs non-responders (PPV=76%, NPV=59% p 0.002) in 1/16. Responders have higher median OS (>54w vs 39w; p<0.05) and higher median DFS (>54w vs 25w; p 0.02) than non-responders, with 5y-OS 91% vs 76% (p. 0.024) and 5y DFS 81% vs 62% (p. 0.002) in 1/16	18F-FDG PET is potentially useful to predict response and outcomes in this setting

Legend Acc: accuracy; AUC: area under the curve; CHT: chemotherapy; CR: complete response; CRT: chemoradiotherapy; ΔCT/ΔPET volume change in lesion volume based on CT or PET measurements; DFS: disease free survival; MA: metanalysis; ΔMRglu: fractional change in MRglu; MTV: metabolic tumor volume; ΔMTV: percentage reduction of the metabolic tumor volume; NPV: negative predictive value; OS: overall survival; pCR: pathologic complete response; PPV: positive predictive value; PD: progression disease; PR: partial response; PROS: prospective; RETR: retrospective; RI: response index; sens: sensitivity; spec: specificity; SD: stable disease; SR: systematic review; TLG: Total Lesion Glycolysis; ΔTLG: percentage reduction of the total lesion glycolysis; TRG: tumor regression grade; VR: visual response; VRA: visual response analysis; VRS: visual response score; w: weeks; y:years

Conclusions: 18F-FDG-PET is a promising imaging system for tumor response prediction and therefore could be used to modulate surgical treatment. However, its accuracy seems insufficient to be used, on its own, as a means of selecting patients for whom surgery should be excluded. Furthermore, thanks to the possibility of predicting overall survival, 18F-FDG-PET could be used to select patients for adjuvant therapies after surgical resection.

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TOTAL NEOADJUVANT TREATMENT IN LOCALLY ADVANCED RECTAL CANCER

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Aims: Determining disease free survival and overall survival with total neoadjuvant approach in patients with local advanced rectal cancer (LARC) is important for stratifying patients according to expected outcomes in future studies in the era of treatment combination. The aims of this analysis were to estimate the pathological complete response, disease free survival (DFS) and overall survival probabilities of rectal cancer patients and to identify predictors of outcomes.

Methods: Studies reporting pathological complete response rate and/or time-dependent outcomes (progression or death) after total neoadjuvant treatment of LARC were identified in MEDLINE through January 2022. Data on patient population and outcomes were extracted from each study by three independent observers and combined using a distribution-free summary survival curve. Primary outcomes were actuarial probabilities of recurrence and survival.

Results: Thirteen LARC treatment studies met the inclusion criteria and 18 total neoadiuvant treatment arms. Pooled estimated of actuarial disease free survival rate was 70.6% (95%CI 62.5-77.7) at 3 years and 65.4% (95%CI 52.5-76.3) at 5 years. Pooled estimate of actuarial survival rates was 93% (95%CI 80.8-97) at 3 years and 81.6% (95%CI 72.1-88.3) at 5 years. Heterogeneity among studies was highly significant for all outcomes.

Conclusions: Pathological complete response, disease free and overall survival are extremely variable in patients with LARC treated with TNT. We found two keys to understanding. We firmly believe that radiotherapy has to be delivered concomitant with chemotherapy (CT) with 5FU or adding oxaliplatin or other different drugs, and number of CT cycles >4 increase substantially the pathological complete response rate and DFS. It's obviously necessary to find a compromise between the efficacy of the therapeutic action and the generated toxicity. This analysis provides an useful benchmark for future comparison and benefits of combination of other drug family as target therapy or immunotherapy.

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NEOADJUVANT RADIO-CHEMOTHERAPY IN RECTAL CANCER: OUTCOMES IN A RETROSPECTIVE MONOISTITUTIONAL STUDY

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Aims: To evaluate Local Control (LC), Overall Survival (OS) and Metastasis Free Survival (MFS) at 2- and 5-years in patients (pts) with histologically confirmed rectal cancer treated with neoadjuvant radio-chemotherapy (RT-CHT), followed by surgery, in a retrospective monoinstitutional study.

Methods: From December 2015 to January 2017, 29 pts affected by rectal cancer were treated with neoadjuvant RT-CHT. All pts underwent intensity-modulated radiotherapy (IMRT) and received 45 Gy in 1.8-Gy daily fractions to the pelvis. Of these, 25 pts were assigned to receive a simultaneous integrated boost of 55 Gy in 2.2-Gy daily fractions to the tumor and positive lymph nodes. The remaining 4 pts received a concomitant boost of 10 Gy in 1-Gy biweekly fractions to the tumor and positive lymph nodes. Concurrent CHT was administered to all these patients, 825 mg/m^2 oral capecitabine twice per day, 5 days per week. After surgery, outcomes were analized in two groups of pts, ypT1-2 (group A – 21 pts) and ypT3 (group B – 8 pts). All data were calculated through Kaplan-Meier curves.

Results: Median age was 59 years (range 40-78). Median survival was 75.8 months (range 25-97 months). In the whole population, at 2- and 5-years LC was 96.6% and 89.3% respectively, MFS 89.5% and 85.9%, OS 96.6% and 86.2% (CI 95%: 80.4-94.5). Specifically, group A showed a 2- and 5-years LC of 100%, group B 87.5% and 54.7% respectively, with a statistically significant difference (p=0.001). At 2- and 5-years OS was 100% in the first group (p value < 0.0001) and 87.5% and 50%, respectively, in the second group.

Conclusions: Our experience showed that neoadjuvant RT-CHT treatment in pts with rectal cancer ensure a high rate of LC, OS, MFS at 2- and 5-years. Especially, OS and LC stay on 100% in group ypT1-2.

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ABSTRACT NOT PUBLISHABLE

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NEOADJUVANT RADIOTHERAPY DOSE ESCALATION WITH SIMULTANEOUS INTEGRATED BOOST (SIB) FOR LOCALLY ADVANCED RECTAL CANCER (LARC); PRELIMINARY RESULTS OF A MONO ISTITUTIONAL CENTRE

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Aims: The aim of this study was to evaluate pathological response, survival rate and toxicity in pts affected by LARC underwent neoadjuvant RT dose escalation in association with Capecitabin.

Methods: From June 2015 to April 2022, 51 patients affected by LARC underwent neoadjuvant RT-CT followed by surgery. The dose prescription was 52,5-55 Gy in 25 ff (45 Gy to the pelvis and 52,5-55 Gy to the T, N+ and mesorectum), given with VMAT- SIB technique. Of them 38 pts (75,5%) received 55 Gy/25 ff and 13 pts 52,5 Gy/25 ff. In association with RT, Capecitabin 1650 mg/mq/day was given. We evaluated survival outcomes and clinicopathological characteristics of Tumour (T), Nodal (N), margins, T and N-downstaging. According to CTCAEvs5 scale acute and late toxicity was evaluated.

Results: At the analysis 30 pts were male (58.8%) and 21 female (41.2%). The median age was 66 years old (range 27-81). After a median follow-up of 40 months (range 3-83mths) estimate Kaplan-Meier survival rate were excellent; OS and PFS were 96% and 90% at 3 years, 88% and 84% at 6 years. Local control resulted 97 % at 6 years of follow-up. Overall, a complete response (CR) as ypT0N0 was obtained in 24% of pts; of them only 2 pts received 52,5 Gy/25 ff. At histological examination a T-CR and a N-CR was observed in 26% and 72,8% of pts. A R0 margins was obtained in all pts (100%). T downstaging and a N-downstaging were observed in 76,5 % and in 90.2% of pts. Overall 5 pts (9,8%) had disease progression; of them 1 pt had local and distant metastases and 3 pts had distant metastases. All pts underwent systemic treatment. Unfortunately we did not find any prognostic factor regarding survival rates and CR. GI and GU G2/G3 acute toxicity was observed in 7 pts (13%), G2 in 9,8 % and G3 in 3,9%. There was not G4 or higher acute or late toxicity. Post-surgical complications were observed in 14 patients (27,4 %); wound dehiscence in 5 pts, fluid collection in 4 pts, infections in 4 and fistula in 1 patient.

Conclusions: Neoadjuvant RT dose escalation 52,5-55 Gy/25ff with VMAT-SIB technique was effective for LARC with high rate of CR, T and N–downstaging. We found low rates of G3 and G2 acute and late toxicity. Randomized trials with higher number of pts and longer follow-up are needed to define better interval time between RT and surgery, prognostic factors to achieve a ypT0N0 and identify patients which can be candidate of wait-and see strategy (pts with ultra low-rectal cancer and cT0N0).

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USE OF TNT FOR LOCALLY ADVANCED RECTAL CANCER IN A REAL-WORLD SETTING

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Aims: The standard of care for Locally Advanced Rectal Cancer (LARC) is preoperative radiation (RT) with or without concurrent chemotherapy. Recently, integration of induction or consolidation chemotherapy to RT (Total Neoadjuvant Therapy, TNT) has been proposed, particularly in patients with high risk features. However, it is unclear whether treatment intensification may be safely applied in advanced cases and the optimal treatment schedule has not been established. We evaluated the feasibility and initial outcome results of this approach in our Radiation Oncology Centre.

Materials and Methods: We retrospectively analyzed a cohort of consecutive patients with LARC treated with TNT at our institution from June 2020 and June 2022. We collected demographics and treatment-related characteristics. Clinical response and treatment-related toxicity were analyzed using descriptive statistics.

Table 1.

Toxicity in induction chemotherapy (n=11)				
	G0	G1	G2	G3-G4
Haematological				
	2	5	4	0
Non haematological				
GE toxicity	2	3	6	0
GU toxicity	10	1	0	0
Cutaneous toxicity	10	1	0	0

Toxicity in combined radiochemotherapy (n=8)				
	G0	G1	G2	G3-G4
Haematological				
	6	2	0	0
Non haematological				
GE toxicity	1	4	3	0
GU toxicity	4	4	0	0
Cutaneous toxicity	7	1	0	0

Results: Eleven patients were found eligible to TNT. Median age was 55 (range 36-64) years. Six patients were males (55%) and 5 were females (45%). Indication to TNT was decided by the multidisciplinary team due to T4 disease (n=1, 9%), N2 involvement (n=4, 36%), or both (n=6, 55%). Colostomy was required in one case due to impending occlusion. All patients received induction chemotherapy consisting of 4 cycles of Folfox or 6 cycles of Folfirinox in 3 (27%) and 8 (73%) patients, respectively. All patients completed the planned treatment schedule: no dose reductions or chemotherapy interruption were required. Adverse events consisted mainly grade (G)≤2 diarrhea and/or transient leucopenia. No grade 3–4 toxic effects were recorded. At the time of our analysis, 8 patients completed chemoradiation and 5 underwent surgery. In 10/11 patients long course chemoradiation to a total dose of 50 Gy in 25 fractions was administered, followed by surgery at 8 weeks from last RT fraction: among operated patients, pathological partial and complete response was obtained in 3 and 1 patient respectively. One patient experienced oligometastatic liver progression after the induction chemotherapy course, requiring short-course RT followed by immediate surgery and subsequently developed multimetastatic disease.

Conclusion: TNT with either Folfox or Folfirinox was feasible and showed a benigne toxicity profile, resulting in no delay to RT and surgery. Early assessment after induction chemotherapy is advised due to risk in-treatment disease progression.

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A CASE SERIES OF WOMEN WITH LOCAL ADVANCED SQUAMOUS CELL CARCINOMA OF THE ANAL CANAL SHOWING COMPLETE RESPONSE DURING FOLLOW UP

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Aims: To report a case series of 5 patients (pts) with locally advanced (LA) squamous cell carcinoma (SCC) of the anal canal who showed complete response (CR) after chemo-radiotherapy (CRT) during a follow-up of 12-72 months. Its treatment is dictated mainly by accurate staging, generally accomplished with a combination of physical examination, endoscopy and biopsy, magnetic resonance (MR), computed tomography (CT), and positron emission tomography (PET). CRT remains the mainstay of treatment with organ preservation and surgery is reserved for salvage therapy. Some studies have indicated that women may have a better prognosis, but there are no data to confirm this in advanced cases.

Methods: From May 2019 to May 2021, we treated 5 female pts (44-74 years old) with LA SCC of the anal canal (cT3cN1M0 stage IIIC). All pts showed voluminous lesions extended from the anal margin to the rectum and suspected lymph nodes in pelvic and inguinal chains. Two pts was HPV+. After a multidisciplinary discussion, they underwent concomitant CRT. CT scheme was mitomycin and 5fluorouracile. RT scheduling was 50Gy

@ 2Gy in 25 fractions to the anal canal, rectum in toto, and mesorectal space; 45Gy @ 1.8Gy in 25 fractions to the pelvic (presacral, iliac internal, external and obturators), inguinal lymph nodes and ischiorectal fossa in 2 pts; with a sequential or simultaneous integrated boost on T and pathological N (total cancer dose to PTV high was 55-60Gy). The CTV high volume ranged from 160 to 295 cc. We used VMAT image-guided daily by CBCT with replanning if necessary. The dose constraints to organs at risk were respected. No treatment was interrupted for toxicity.

Results: After treatment, all pts referred dysuria and vaginal discomfort G1; diarrhoea, tenesmus and skin lysis G2. Currently, for all, the follow-up examination (MR, PET and endoscopic exam) shows CR. No pt reports chronic toxicity greater than G1 and all report good performance of both anal sphincters.

Conclusions: This series confirms that concomitant CRT is the best therapeutic strategy in the treatment of SCC of the anal canal to maintain proper organ function over time even in LA disease. It is interesting that 5 consecutive cases of women with LA disease obtained persistent CR.

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MONO-INSTITUTIONAL SERIES OF 45 PATIENTS TREATED WITH STEREOTACTIC RE-IRRADIATION FOR ISOLATED LOCAL RECURRENCE OF PROSTATE CANCER AFTER PRIMARY SURGERY AND SALVAGE OR ADJUVANT RADIOTHERAPY

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Aims: Re-irradiation by SBRT represents a valid option for treating locally recurrent prostate cancer (PCa). The aim of this retrospective study was to determine the efficacy and safety of such treatment.

Methods: The study included patients who underwent salvage radiotherapy for isolated PCa local recurrence after primary surgery and previous salvage/adjuvant radiotherapy or brachytherapy at our Institution between 2010 and 2021. Patients who received hormone therapy and those who underwent more than one local re-irradiation were also included. Local relapse in the prostate bed was assessed by MRI and/or choline or PSMA-PET. Histological confirmation was not mandatory. Salvage SBRT re-irradiation was delivered with IGRT using the BrainLab VERO System.

Results: Forty-five patients met the inclusion criteria and were included in the study (Table 1). Most lesions (29, 64.4%) were peri-anastomotic. PET was available for 25 (55.5%) and MRI for 39 (86.7%) patients. Five patients (11.1%) received more than one SBRT treatment for prostate bed recurrence, with one of them (2.2%) receiving three re-irradiations. Among the 38 patients with updated follow-up data, 8 (21.1%) resulted free from disease at last contact. Progression of disease was observed in 30 out of 38 patients (78.9%) with 16 clinical and 14 biochemical progressions. Median time to clinical and biochemical progression were, respectively, 15.5 (IQR: 10.7–21.9) and 14.0 months (IQR: 10.7–41.9). Of them, only one patient experienced polyprogression. Regarding acute toxicity outcomes, no genitourinary (GU) events higher than grade (G) 1 and no gastrointestinal (GI) events higher than G2 occurred. During follow-up, no patients but three experienced GU/GI events higher than 2. One patient had G3 GU maximum toxicity with implantation of an artificial urinary sphincter after worsening of urinary incontinence, which however decreased to G0 at last contact. Two patients experienced late G4 GU toxicity: one of them had acute urinary retention with bladder catheter positioning, the other one underwent internal urethrotomy. For the former, toxicity grade decreased to G2 at last follow-up. None of the patients experienced late GI toxicity.

Conclusions: Salvage stereotactic re-irradiation treatment for locally recurrent PCa seems to be a safe and promising strategy to control bed recurrence. Further studies and longer follow-ups are warranted to confirm these preliminary findings.

Table 1. Patients and SBRT re-irradiation treatment characteristics.

Patients characteristics	**Age at 1st re-SBRT** *years, median (IQR)*		67.0 (65.2– 74.8)
	CCI at re-SBRT		5.5 (4 – 6)
	Time between first RT and re-SBRT *years, median (IQR)*		14 (7.3 – 34.6)
	iPSA *ng/ml, median (IQR)*		8.5 (5.45 – 14.37) *
	pT	**2**	17 (37.8%)
		3	24 (53.3%)
		NA	4 (8.9%)
	pN	**0**	24 (53.4%)
		1	5 (11.1%)
		NX	14 (31.1%)
		NA	2 (4.4%)
	ISUP grade	**1**	6
		2	13
		3	5
		4	6
		5	10
		NA	5
	rPSA *ng/ml, median (IQR)*		1.8 (1.1 – 3.8)
	Follow-up *months, median (IQR)*		16.9 (10.57 – 55.72) **
Treatment characteristics	**Number of fractions**		5
	Total dose *Gy, median (IQR)*		30 (25 – 35)
	BED *Gy, median (IQR)*		150.0 (108.3 – 198.3)

*Missing data for 3 patients; ** Missing data for 5 patients; Abbreviations: BED (biological equivalent dose); CCI (Charlson Comorbidity Index); iPSA (Initial Prostate Specific Antigen); ISUP (International Society of Urological Pathology); NA (not available); PET (Positron Emission Tomography); pN (pathological N); pT (pathological T); re-SBRT (Re-irradiation by stereotactic body radiotherapy); rPSA (PSA at recurrence); RT (radiotherapy).*

P210

LONG-TERM RESULTS OF HIGH-QUALITY LINAC-BASED STEREOTACTIC BODY RADIATION THERAPY WITH FLATTENING FILTER FREE BEAMS AND VOLUMETRIC MODULATED ARC THERAPY FOR LOW-INTERMEDIATE RISK PROSTATE CANCER

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Aims: In 2016 we published a phase II study exploring safety and efficacy of Stereotactic Body Radiation Therapy (SBRT) delivered with Volumetric Modulated Arc Therapy (VMAT) and Flattening Filter Free (FFF) beams in prostate cancer patients. We present herein the updated results on late toxicity and long-term survival.

Methods: Patients enrolled in the study had a biopsy-confirmed localized prostate cancer and the features of a low- or intermediate-risk disease (NCCN criteria). The radiotherapy schedule consisted of 35 Gy delivered in 5 fractions every other day. Toxicities were registered according to the CTCAE v4.0. Biochemical recurrence was defined as an increase of PSA after nadir, confirmed at least once. Local Recurrence (LR) and Distant Metastases were detected either with Choline- or PSMA-PET/CT scans. Survival analysis, in terms of Biochemical Recurrence-Free Survival (BFS), Local Control (LC), Distant Metastasis Free Survival (DMFS) and Cancer Specific Survival (CSS), were performed by Kaplan-Meier curves using MedCalc.

Results: Ninety patients were submitted to SBRT between February 2012 and March 2015. Median age was 71 years (range 48-82). Fifty-eight patients (64.5%) had a Gleason Score of 6, while 32 (35.5%) had a Gleason Score of 7. According to the 2014 WHO-ISUP Grade Group System, 58 patients were classified as GG1 (64.5%), 21 patients as GG2 (23.3%), 11 as GG3 (12.2%). A late grade 1 Genito-Urinary toxicity was observed in 50% of patients while a grade 2 in 3.3%. A late Gastro-intestinal grade 1 toxicity was reported in 19% of patients, while a grade 2 in 2.2%. No heavier toxicities were observed. At a median follow-up of 102 months (range 7-123), 5- and 8-year BFS were 93.0% and 85.4% respectively, 5- and 8-year LC were 95.3% and 88.7% respectively, 5- and 8-year DMFS were 95.3% and 90.1% respectively. In our series, the 11 patients with an ISUP Grade Group 3 disease experienced a significantly worse outcome (5- and 8-year BFS were 66.7% and 33.3% respectively, 5- and 8-year LC were 77.8% and 53.3% respectively, 5- and 8-year DMFS were 77.8% and 41.7% respectively, p=0.001). Sixteen patients were dead at the moment of our analysis, but only one died from prostate cancer, 102 months after treatment.

Conclusions: This long-term update confirms that SBRT is a valid therapeutic strategy for low-intermediate risk prostate cancer. High quality radiotherapy with VMAT and FFF warrants optimal results in terms of toxicity and disease control.

P211

1.5T MR-GUIDED RADIOTHERAPY *VERSUS* LINAC-BASED VOLUMETRIC-MODULATED ARC STEREOTACTIC BODY RADIOTHERAPY IN THE TREATMENT OF LOCALIZED PROSTATE CANCER: A TOXICITY COMPARATIVE ANALYSIS

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Aim: To compare acute toxicity of prostate cancer (PCa) stereotactic body radiotherapy (SBRT) delivered by MR-guided radiotherapy (MRgRT) with 1.5T MR-linac (MRgRT) or by volumetric modulated arc (VMAT) with linac.

Methods: Patients with histologically diagnosed low-to-intermediate risk class PCa were treated with exclusive SBRT. The schedule in 5 fractions were 35 Gy and 36.25 Gy for low and intermediate risk class, respectively. Patients treated with MRgRT were enrolled in an ongoing Ethical Committee (EC) approved trial (n° 23748), while patients treated with linac-based SBRT were enrolled in an EC approved PCa SBRT phase II trial (n° SBRT PROG112CESC). The primary end-point was acute toxicity. Patients were included in the analysis if they had at least 6 months of follow-up for the acute toxicity end-point evaluation. Toxicity assessment was performed according to CTCAE v5.0 scale. International Prostatic Symptoms Score (IPSS) was also performed.

Results: 137 patients were included in the analysis. 57 (41.6%) were treated with MRgRT, and 80 with conventional linac. The median initial PSA before RT was 6.5 ng/ml (range 1-19). Globally, acute G1, G2, and G3 toxicity occurred in 32 (23.3%) 20 (14.5%), and 4 (2.8%) patients. At the univariate analysis acute G1 did not differs significantly between MRgRT and linac (23.75% versus 21%; p=n.s.), while G2 toxicity was significantly lower in the MRgRT group (4.5% versus 10%; p=0.032). Acute G2 gastrointestinal (GI) toxicity occurred in 7% and 7.5% of MRgRT and linac group (p=0.61), while acute G2 genitourinary (GU) toxicity occurred in 10.5% and 15% of MRgRT and linac group (p=0.004). The median IPSS before and after SBRT was 3 (1-16) and 5 (1-18). Acute G3 toxicity occurred in 2 in the MRgRT and 2 in the linac group (p=n.s.).

Conclusion: Prostate SBRT with 1.5TMR-linac is feasible and safe. Compared to linac-based SBRT, MRgRT seems characterized by a reduced incidence of grade 2 toxicity. A longer follow-up and a larger population is needed to confirm these preliminary data.

P212

EARLY TOXICITY AND DIFFUSION-WEIGHTED MRI ASSESSMENT AFTER SINGLE-DOSE ABLATIVE RADIATION THERAPY FOR ORGAN-CONFINED UNFAVORABLE PROSTATE CANCER

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Aims: To investigate diffusion-weighted (DWI) MRI changes and early gastrointestinal (GI) and genitourinary (GU) side effects in patients with organ-confined unfavorable prostate cancer (PCa) following Single-Dose Ablative Radiation Therapy (SDART).

Method: Ten patients included in the prospective clinical trial "ABRUPT" (NCT04831983) were treated with a single fraction of 24 Gy to the whole prostate with urethra sparing in association with androgen deprivation therapy (ADT) as per standard of care. Treatment was delivered on Linac platform with a Volumetric Modulated Arc Therapy (VMAT) and a real-time organ-motion electromagnetic tracking system. Multiparametric MRI was performed before SDART (time 0), one-hour post-SDART (time 1), and 3-month after treatment (time 2). Acute toxicity was evaluated with Common Terminology Criteria for Adverse Events version 5 (CTCAE_v5) scale. IPSS score and quality of life (QoL) metrics assessed with EORTC questionnaires QLQ-PR25/-C30 were also measured.

Results: Median age was 76 years (range 62-82). Median prostate volume was 35.4 cc (range 10-59). At 3-months follow-up none of the patients experienced GI toxicity, while GU side effects were observed only in three patients (two G1 and one G2). Median IPSS score decreased from 6 (range 2-8) at baseline to 5 (range 2-17) 3 months after treatment. At the same timepoints no significant changes in EORTC-QoL score were documented. An increase of ADC value of tumor lesion by about 26% (range 7%-66%) and 51% (range 21%-81%) was registered at time 1 and time 2 respectively, compared to the baseline. Median prostate volume was found unchanged at time 1, while decreased by about 25% (range 9%-59%) at time 2. At last follow up all patients were found bNED, and four of them had a complete response.

Conclusions: SDART irradiation of the whole prostate with urethra sparing was feasible and well tolerated. Our findings showed a correlation between early changes in ADC values after SDART and later tumor response in patients with unfavorable PCa. Long term results are needed to confirm whether DWI can be used as an early biomarker of treatment outcome in this setting.

P213

PSMA PET/CT IN THE MULTIDISCIPLINARY DECISION-MAKING PROCESS IN MEN WITH BIOCHEMICAL RECURRENCE OF PROSTATE CANCER

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Aims: Prostate-specific membrane antigen (PSMA) PET/CT is highly sensitive in identifying the site of recurrence in men with biochemical recurrence (BCR) after primary therapy for prostate cancer. Precise determination of disease extent plays a fundamental role for tailored made therapy. The purpose of our study was to assess the impact of PSMA PET/CT on patient management and to report prostate-specific antigen (PSA) response after PSMA-guided radiotherapy.

Method: Between February 2021 and July 2021, 41 patients with BCR were studied by PSMA PET/CT, who were candidates to salvage therapy. Oligorecurrent prostate cancers were treated with image-guided radiotherapy of their metastases. Sites of relapse were characterized, the proportion of patients in whom management changed, and the proportion of patients in whom outcome measure was obtained were reported.

Results: The primary treatment was radical prostatectomy or definitive radiotherapy in 85% and 15% of cases, respectively. Median PSA level at PSMA PET/CT was 0,63 ng/ml (0,11-6,9 ng/ml; Q3=1,4 ng/ml). Grade group was 2, 3 and 4 in 33%, 28% and 15% of patients, respectively. PSMA PET/CT was positive in 31/41 (76%), for a total of 61 metastases. Bone and nodal metastases were found in 45 and 23% of patients, respectively. PSMA PET/CT findings changed the treatment choice in 53% of patients, 73% (Figure 1) of which were treated with stereotactic body radiotherapy (SBRT), 24-36 Gy in 3-6 fractions. After PSMA-guided radiotherapy, a biochemical response was detected in 56% of the cohort. No relevant toxicities were registered.

Conclusions: PSMA PET/CT allows detection of recurrence sites in more than 2/3 of men with BCR and impacts patient management in more than half of the men avoiding empirical treatment, such as prostate bed radiotherapy or androgen deprivation therapy. The available evidence suggests that SBRT is a cost-effective

approach for oligometastatic disease but prudent selections of patients is very important. Studies being in progress and future trials will clarify whether PSMA-guided radiotherapy will be the new gold standard technic for specific groups of patients.

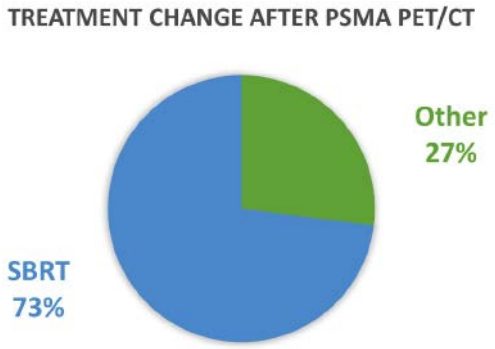

Figure 1.

P214

SINGLE-PATIENT MICROBIOTA & INFLAMMATION PROFILES MODULATE DOSE-RESPONSE CURVES FOR ACUTE TOXICITY

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Aims: A mono-institutional trial investigated the role of gut microbiota (MB) and inflammation markers (cytokines) in driving toxicity (tox) after radiotherapy (RT) for prostate cancer (PC). To establish personalised predictive models, we focused on introducing MB and cytokines into Normal Tissue Complication Probability models (NTCP) for acute tox.

Method: We enrolled 135 consecutive patients (pts) receiving conventional (78Gy/2Gy) or hypo (65Gy/2.6Gy) RT. A population of 70 PC pts was accrued to validate findings on MB. Evaluation was done pre, during & at RT end, including gut MB measures (16S sequencing & pooling in Operational Taxonomic Units - OTUs- with Uclust software) and blood assessment of cytokines (CCL2, TGFβ, TNFα, TNFR1, PDGF). Tox was scored weakly using CTCAE. Average grade>1.3 for intestinal tox during RT (aGI) was the endpoint for this analysis.We used multivariable logistic regression (LR) to derive inflammation signatures (based on cytokine levels at baseline) and unsupervised clustering (fuzzy c-means) to partition pts into MB clusters based on the relative abundance of OTUs before RT start. Information on inflammation & MB clustering was introduced as a dose-modifying factor into a logit NTCP model.

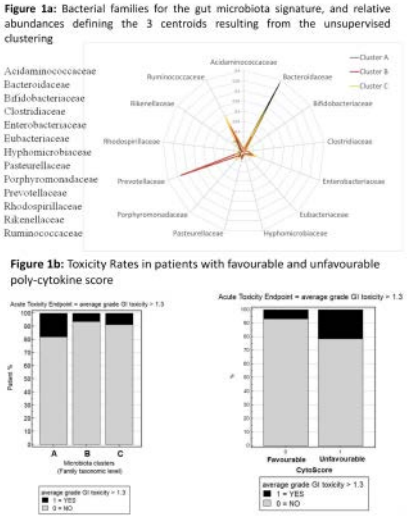

Figure 1.

Figure 2: ROC curves for the NTCP model including only the mean rectal dose and the model including information from stratification of patients based on microbiota and inflammation markers

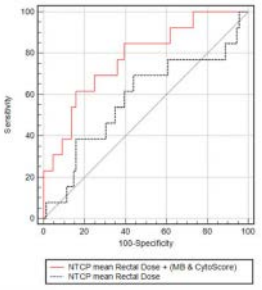

Figure 2.

Results: 16/135 tox events were scored. Baseline levels of PDGF, TGFβ1 & TNFα were significantly associated with aGI: we developed an LR-based poly-cytokine risk score for aGI (CytoScore, OR=2, p=0.01, AUC=0.67). MB clustered in 3 groups at the Family taxonomic level, with 13 families included in the centroid signature (Figure 1a). Pts in cluster A had a significantly higher probability of aGI tox [unfavourable (unf) MB] compared to pts in clusters B and C [favourable (fav)

MB]: tox rates were 17.9 vs 7.6%, OR=2.6 (p=0.05, Figure 1b). MB clustering was confirmed in the validation cohort: tox rates 13 vs 8% in unf vs fav MB. We classified pts at low-risk (LR) of tox if they had "fav MB AND Cytoscore", at intermediate-risk (IR) if "fav MB OR Cytoscore", at high-risk (HR) if "unf MB AND Cytoscore". Observed tox rates in LR/IR/HR were 3/10/35% (p=0.003). NTCP model including only mean rectal dose had AUC=0.53. Introducing pts stratification from MB & CytoScore NTCP model had AUC=0.78 (Figure 2).

Conclusions: We determined 3 risk classes for RT-induced aGI effects based on the combination of MB information and cytokine profiles. The personalised NTCP, including this stratification, had increased discrimination. This represents a relevant finding for the prediction of tox.

P215

THE ROLE OF INFLAMMATORY INDICES IN MCRPC PATIENTS: CAN THE HEI INDEX (HEMO-EOSINOPHIL INFLAMMATION INDEX) HAVE A POTENTIAL PROGNOSTIC VALUE? A BI-INSTITUTIONAL EXPERIENCE

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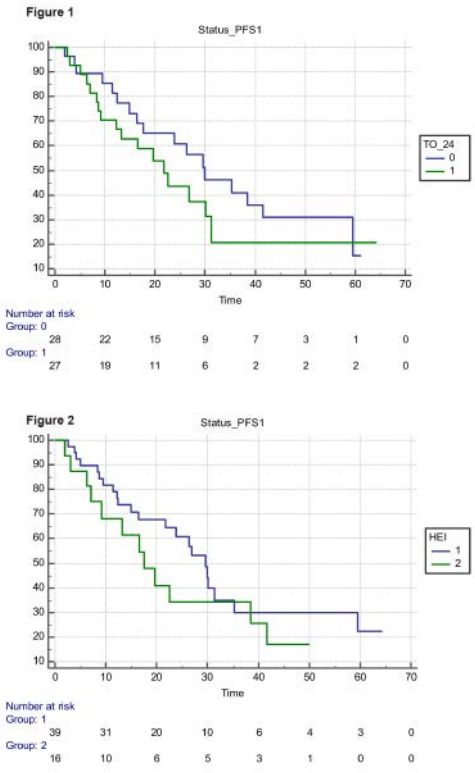
Aims: Recently, the hemo-eosinophilis inflammation (HEI) index has shown a prognostic role in anal cancer. On the basis of these evidences, our aim is to evaluate whether this simple scoring system can be correlated with prognosis in patients with metastatic castration-resistant prostate cancer (mCRPC).

Methods: We pooled data relating to mCRPC patients in androgen receptor targeted agents (ARTA) therapy from two participating centers and analyzed them retrospectively. Full blood tests were collected before starting ARTA therapy and blood count baseline were used to calculate inflammation indices. HEI index is a prognostic score system based on laboratory inflammation parameters and is evaluated considering a weight= 1 for each of the following variables: hemoglobin levels < 12 g/dl, immune-inflammation index (SII, which is neutrophil-to-lymphocyte ratio -NLR- x platelets) >560 and eosinophil count ≥100/µl. All patients were stratified according to the HEI Index into two different risk groups: low-risk (from 0 to 1 negative prognostic factor) and high-risk (from 2 to 3 negative prognostic factors). In addition, patients were stratified by ISUP at diagnosis and duration of response to first androgen deprivation therapy (ADT). Kaplan-Meier survival curves were used for PFS1, which is calculated from the initiation of ARTA to disease progression, defined as adding radiotherapy to oligoprogressive sites or change/definitive end of systemic treatment.

Results: A total of 54 mCRPC patients were analyzed and treated with ARTA, of these 34(63%) received abiraterone plus prednisone and 20(37%) received enzalutamide. According to ISUP Classification, 6(11%) patients were PGG 1, 7(12%) PGG 2, 13(24%) PGG 3, 16(29.6%) PGG 4 and 11(20.4%) PGG 5. 26 patients (48.1%) received hormone therapy for less than 24 months before starting ARTA therapy. Based on HEI Index, the low-risk group consisted of 38 patients, while 16 patients were assigned to the high-risk group. The median PFS1 was 29.6 months in the low-risk group and 26.3 months in high risk group (HR: 0.65 (95%CI 0.3-1.4), p=0.27) (Figure 1). In according to duration of response to first ADT, the median PFS1 was 30 *vs* 21.8 (duration TO >24 months and < 24 months, respectively) (HR: 0,71 (95%CI 0,36 to 1,43), P=0.34) (Figure 2).

Conclusions: Our results proved not statistically significant but, as can be seen from Kaplan-Meier survival curves, PFS1 seems to have a trend in favor of patients with low risk HEI index and in long-term responders of ADT.

Figures 1 and 2.



P216

UPDATE ON USE OF HELICAL TOMOTHERAPY IN THE DEFINITIVE TREATMENT OF UNFIT BLADDER CANCER PATIENTS FOR SURGERY: A MONO-INSTITUTIONAL STUDY (2011-2021)

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Aims: To evaluate use of Helical Tomotherapy (HT) in the treatment of bladder cancer. The HT system employs a compact 6 MV Linac-based on CT ring gantry to rotationally deliver intensity modulated fan beams. The HT unit also contains a mega-voltage CT detector array located opposite the radiation source for pre-treatment verification, allowing accurate re-positioning. This technique permits to precisely target tumors minimizing impact on surrounding healthy tissue: this could be very interesting for unfit bladder patients, to reduce GU and GI toxicity.

Methods: 47 patients (age:52-88) with bladder cancer were treated from January2011 to December 2021. None of these patients were fit for surgical indication due to concomitant medical conditions. None of these patients had concomitant chemotherapy due to medical conditions. 28/47 (59%) of these patient had positive lymphonodes. The radiation oncologists contoured the volumes of interest (CTV) according to the RTOG guidelines. The planning target volume (PTV) was generated from the CTV volume by adding a 3 mm margin in all directions. Accurate delineation of organ at risk was performed. In these patients, we used several radiotherapy schedules (45 Gy, 40 Gy, 60 Gy, 50 Gy, 54 Gy) , according to volume (Whole bladder while elective treatment to the lymph nodes was optional taking into account patient comorbidities and the risks of toxicity) and site of cancer and considering PS of the patients. Treatment plans were evaluated on a dedicated TPS.

Results: 41/47 of these patients ended scheduled radiotherapy: 4 patients ended early treatment for cardiac condition, 2 for diabetes complications. Median follow up was about 18 months (range 2-52). All patients had acute GU toxicity: 26 patients (63%) had G1, 10 patients (25%) had G2 and 5 patients (12%) had G3. Late GU toxicity was seen in 11 patients (26%) as G1 and in 3 patients (7%) as G2. 22 patients (55%) had GI toxicity: 19 patients (86%) had G1, 3 patients (14%) had G2.Late GI toxicity was seen in 6 patients (15%) as G1. OS was 79% at 1 years, 66% at 2 years and 41% at 3 years, 25% at 4 Years.

Conclusions: HT is a safe and feasible technique to treat unfit patients for surgery. All patients had acute GU toxicity, but it was acceptable for the greatest part of them. Acute GI toxicity was acceptable too. Late toxicity, both GU than GI, was never ≥G3. The OS is satisfying but surely influenced by the poor clinical concomitant conditions of the patients too.

P217

LINAC-BASED EXCLUSIVE STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR PROSTATE CANCER (PCA): LONG-TERM OUTCOMES OF A MONO-INSTITUTIONAL EXPERIENCE

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Aims: The aim of this study was to evaluate outcomes of a large series of PCa patients treated with exclusive SBRT without the addition of androgen deprivation therapy (ADT).

Methods: We retrospectively analysed a prospective database on 80 PCa patients treated with SBRT consisting in 42 Gy/7 fractions, 3 days per week between January 2013 and June 2020. Patients were treated with volumetric-modulated arc therapy (VMAT) with conventional and flattening-filter-free 6 MV photon beams. Image-guidance was performed with intraprostatic gold fiducial markers. No patients received any ADT. Oncological endpoints were: biochemical progression-free survival (bPFS), metastasis-free survival (MFS), local control (LC) and cancer specific survival (CSS). Biochemical recurrence was defined according to Phoenix criteria (nadir +2 ng/mL). Survival analysis was performed using the Kaplan-Meier method and the log rank test was applied to compare the effect of the individual variables (age, Gleason score, initial PSA, tumour node metastasis (TNM) stage, NCCN risk classification) on different outcomes. Acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were graded using the Common Terminology Criteria for Adverse Events,version 5.0.

Results: Median follow up was 52 months (range 24-114 months), with 30 patients followed for at least 5 years. Twenty-two (28%), 20 (25%), 21 (26%), 13 (16%) and 4 (5%) patients were classified as very low-risk (VLR), low-risk (LR), favourable-intermediate-risk (FIR), unfavourable-intermediate-risk (UIR), and high-risk (HR) group according to the NCCN risk classification, respectively. Patient characteristics are shown in Table 1. For the entire group, 5-year bPFS was 91%, MFS was 95%, local control was 98%, and CSS was 100%. No statistically significant differences were observed among the individual variables analysed on the different outcomes. There were no acute nor late grade ≥3 toxicities. We reported 1 (1%) and 27 (34%) acute grade 2 GI and GU toxicities respectively. Only one late grade 2 GU toxicity was observed.

Conclusions: SBRT in 7 fractions without ADT

represents an effective and safe treatment. Further studies are needed to test the efficacy of exclusive SBRT for UIR and HR prostate cancer.

Table 1.

Table 1: Patients baseline characteristics

Characteristics	N° 80 (%)
Age median (range)	74 (80-57)
>70	59 (74)
<70	21 (26)
ISUP grade	
1	48 (60)
2	29 (36)
3	2 (2,5)
4	1 (1,5)
PSA at diagnosis	
<10 ng/ml	70 (87,5)
10-20 ng/ml	8 (10)
>20 ng/ml	2 (2,5)
T stage	
cT1c-2a	74 (92)
cT2b-2c	5 (6,5)
cT3a-3b	1 (1,5)
NCCN risk	
VLR	22 (28)
LR	20 (25)
FIR	21 (26)
UIR	13 (16)
HR	4 (5)

P218

LOW DOSE RATE BRACHITHERAPY (LDR-BRT) IN THE ELDERLY PATIENT WITH LOCALIZED PROSTATIC CANCER: THE IMPORTANCE OF PATIENTS SELECTION AND IMPLANT QUALITY

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Aims: This study investigated the results on biochemical relapse-free survival (b-DFS) and Genitourinary (GU)-Gastrointestinal(GI) Toxicity (TOX) by evaluating the importance of factors related to disease and treatment.

Method: From September 2019 to January 2022, 32 patients (pt), aged ≥ 75 years, with clinically localized prostate cancer, low/favorable-intermediate risk category, were treated whit LDR-BRT trans-rectal-echo-guided-approach, as monotherapy, with the permanent-implant-prostate of radioactive-seeds of I125. The eligibility criteria were: a good performance status (Karnofsky index ≥ 70) and a life expectancy greater than 5 years. Treatment planning was carried in the operating room under spinal or total anesthesia, using a dedicated planning-system (TPS) VariSeed 8.0.2. Dose prescription D90 to the prostate was 160-180 Gy. Prostate and Organ at Risk (OAR), urethra and rectum, were contoured according to European-Society-for-Therapeutic-Radiology-and-Oncology-(ESTRO) guidelines. The dose constraints for the anterior rectal wall were D2cc <100%, D0.1cc <150%, D90 <80 Gy, V100 <1.3 cc, for the urethra D10 <150%, D30 <130% (<240 Gy). Follow-up (FU) was performed every 3 months during the first year and every 6 months in subsequent years, assessing PSA levels, acute and late TOX. The primary end-point of the study was the evaluation of b-DFS. Biochemical recurrence was defined according to Phoenix definition (PSA nadir+2ng/ml), calculated from the date of implant to the last FU. The secondary end-point was the evaluation of TOX GU and GI using the toxicity-scales of the Radiation-Therapy-Oncology-Group (RTOG).

Results: The distribution of pt according to risk groups was: 19 at low risk and 13 at intermediate risk. At the last FU, all 32 pt were free from b-DFS. Acute TOX GU was G1-G2 in 28 pt, Acute TOX GI was G1-G2 in 13 pt, Late TOX GU was G1-G2 in 16 pt, Late TOX GI was G1-G2 in 18 pt. No TOX GU-GI acute and late G3 was detected. The study confirms that the implant quality, an optimal dose at CTV (≥ 140 Gy) and the postimplant dosimetry distribution (valuated 1 month after performing the pelvic CT) affect the results of the primary endpoints (b-DFS) and secondary (acute and late TOX).

Conclusions: This study confirm the importance of quality implant in elderly patients with low/favorable-intermediate risk prostate cancer. A longer follow-up will allow to confirm the results obtained. LDR-BRT is effective and well tolerated technique.

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BENEFIT OF DAILY ONLINE CBCT-BASED ADAPTIVE RADIOTHERAPY IN PROSTATE CANCER: A PRELIMINARY ANALYSIS

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Aims: The aim of this study was to evaluate the benefit and the potentialities on a dosimetric point of view of online daily adaptation in prostate cancer by using a modern CBCT-based linac able to provide online adaptive radiotherapy (online ART) using Artificial Intelligence (AI) system.

Method: A total of 8 patients affected by prostate cancer and treated with online ART were enrolled for this study. All the patients received a radiotherapy treatment on an AI-based Linac (Ethos, Varian, US) consisting of 67.5 Gy administered in 25 fractions. CTV was defined as

prostate and seminal vesicles (according to disease stage), PTV as 5 mm CTV expansion. For each patient a daily CBCT was acquired, and a daily online adaptive workflow was performed in collaboration among a radiation oncologist (RO), a medical physicist and a radiation therapist. Organs at risks (rectum, bladder, bowel) were automatically segmented by the AI-system and online checked by the RO, therapy volumes (CTV and PTV) were manually delineated. Treatment plan was automatically reoptimized by the system and two treatment plans were created: a predicted one, consisting in the calculation of the original fluence on the daily anatomy, and an adapted one, result of a new optimisation. DVH indicators were daily recorded for PTV (V95% and V105%), bladder (V65Gy), bowel (V45Gy) and rectum (V50Gy) considering the adapted and predicted plan. The difference among predicted and adapted indicators were investigated using the Wilcoxon Mann Whitney test for paired sample. Significance was considered in case of p-value less than 0.05.

Results: A total of 118 fractions were analysed. Without online adaptation the mean V95% of PTV was 86.4%, while using online adaptation a mean value of 98.4±1.1% was obtained: the difference between the two modalities resulted to be statistically significant ($p<0.01$). As regards OARs, no significant difference was observed in terms of dose sparing (probably due to the patient preparation procedures), but a reduction in terms of dose variation was found for bladder and rectum when adapted plan was used: the whole data are reported in Figure 1.

Conclusions: On a dosimetric point of view, the results of this preliminar analysis shows that performing daily adaptation in prostate leads to a statistically significant gain in PTV coverage (V95%), with similar risk in terms of toxicity for surrounding OARs, where similar dose values were observed.

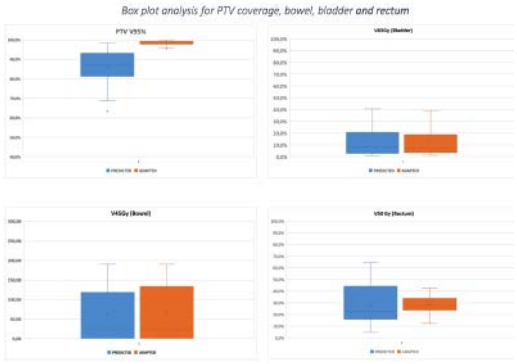

Figure 1.

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EVALUATION OF RECTUM AND BLADDER DOSIMETRIC CHANGES DURING INTRAFRACTION PROSTATE SHIFTS DETECTED WITH ELEKTA CLARITY DURING PROSTATE CANCER TREATMENT

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Aims: Through the analysis of DVHs related to PTVs and organs at risk (OARs) of an initial series of patients treated at our center, the present work aims to correlate intra-fraction movements of the prostate to dosimetric changes using the Clarity Elekta ultrasound system.

Methods: Five patients, with stage I-II prostate adenocarcinoma and recruited on the basis of compliance, were involved in the study. The fractionation scheme applied was 60Gy/20fr, and the dosimetric constraints adopted are shown in Table 1. First, we verified that prostate displacements over time, found during treatment sessions by the Clarity system, were in agreement with data from the literature.[1] Then, assuming hypofractionation schemes at higher doses/fractions, and thus longer treatment times, we simulated at TPS the displacements, (95% CI), corresponding to times of 5, 10 and 20 minutes. Both PTVs and major OARs (rectum, rectum wall, and bladder) were then rigidly translated without deformation by 5, 7, and 9 mm in every direction along the observed shifts for each patient.

Table 1.

ORGANS AT RISK		
BLADDER	RECTUM	RECTUM WALL
V_{41Gy}<50%	V_{46Gy}<30%	V_{32Gy}<50%
V_{48Gy}<25%	V_{37Gy}<50%	V_{50Gy}<25.8%
V_{60Gy}<5%		V_{60Gy}<10%

Results: From the analysis of the DVHs of each patient, the trends of the dosimetric constraints as a function of the simulated displacements were reported, and the minimum displacement for which some of them were no longer satisfied was identified. We showed that the maximum threshold not to be exceeded was 3 mm in terms of Euclidean distance. We then proceeded to decompose this vector into its Cartesian components derived from the Clarity system data for each patient: the results showed that about 2 mm approximately in ANT/POS and INF/SUP and 1 mm in RIGHT/LEFT are the best margins to achieve compliance with the above criteria.

Conclusions: Aware of the very limited set of cases considered in our study, we can conclude that the use of a

"real-time tracking system" such as Clarity Elekta allows us to apply expansion margins to the CTV to obtain the PTV of only 3 mm, reducing the dose to the OARs without penalizing the target volume.

Reference

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A RANDOMIZED CONTROLLED TRIAL ON LIFESTYLE AND INTERACTION WITH MICROBIOTA IN PROSTATE CANCER PATIENTS UNDERGOING RADIOTHERAPY: MICROSTYLE STUDY

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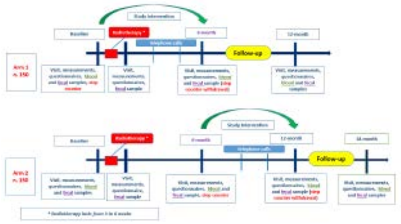
Aim: To report preliminary data from MICROSTYLE study, a clinical trial for prostate cancer (PCa) patients (pts) undergoing RT designed to investigate whether changes towards a healthy lifestyle are able to modify microbiome, improve quality of life and decrease the side effects of RT.

Methods: According to the study protocol 300 PCa pts undergoing adjuvant/salvage or curative RT will be recruited in two comprehensive Italian Cancer Centers. Participants will be randomized in two arms: Intervention Group (IG) and Control Group (CG); the ones allocated to the IG will receive personalized counseling on diet and exercise to improve overall lifestyle and to reduce eventual RT-related toxicities and a steps counter to monitor and increase physical activity reducing sedentary behavior. Participants included in the CG will receive baseline general advice and materials available for pts undergoing RT. The primary outcome will be assessed after a 6-month intervention, by measuring the change in adherence to a healthy lifestyle. As secondary outcomes, the change from baseline in fasting serum metabolic and inflammatory biomarkers will be monitored. Intestinal microbiome composition will be evaluated trough fecal samples analyses. According to the cross-over design, the CG will cross to the IG after 6 months, to actively enhance compliance towards suggested lifestyle recommendations for all pts (Figure 1a).

Results: Recruitment started on October 2021 and to date, 48 pts have been enrolled (22 allocated to IG and 26 to CG) with a median age at recruitment of 70 years (IQR 11). Baseline characteristics of the pts with available data (n=27) are reported in Figure 1b. Twenty-three pts completed the RT course (13 in the IG and 10 in the CG). Of them, 16 underwent an exclusive curative RT treatment while 7 underwent adjuvant/salvage RT. No acute grade (G) >2 genitourinary (GU) and gastrointestinal (GI) toxicities were observed among both arms. A total of 71 fecal samples have been collected (48 baseline + 23 end of RT).

Conclusion: This innovative trial proposes a lifestyle intervention during RT, which includes both dietary and physical activity counselling, as well as monitoring changes in microbiome and serum biomarkers. The promotion of healthy behavior will be started before initiation of standard care, to achieve long lasting impacts, control side effects, coping with feelings of anxiety and depression and improve the effectiveness of RT.

a)



b)

Variable	N.	ALL, n (%) 27	IG, n (%) 15	CG, n (%) 12
ISUP group	1	6 (22)	5 (33)	1 (8)
	2	13 (48)	5 (33)	8 (67)
	3	4 (15)	3 (20)	1 (8)
	4	2 (7)	1 (7)	1 (8)
	5	2 (7)	1 (7)	1 (8)
PSA (ng/ml)	Median (IQR)	6.8 (7.3)	6.1 (6.3)	7.6 (7.7)
BMI (kg/m²)	Median (IQR)	27.2 (5.8)	27.8 (7.3)	26.5(4.1)
WHR	Median (IQR)	0.99 (0.08)	1.01 (0.08)	0.98 (0.09)
Glycemia (mg/dl)	Median (IQR)	98.5 (20.0)	100.0 (18.8)	93.5 (21.0)
Triglyceride (mg/dl)	Median (IQR)	97.0 (41.3)	88.5 (53.0)	97.0 (30.8)
Total cholesterol (mg/dl)	Median (IQR)	187.0 (33.5)	181.0 (61.0)	188.5 (27.0)
HDL cholesterol (mg/dl)	Median (IQR)	50.5 (15.5)	50.0 (13.0)	51.0 (17.0)
LDL cholesterol (mg/dl)	Median (IQR)	112.0 (22.8)	112.0 (49.0)	112.0 (17.0)

*List of abbreviations: **BMI:** body mass index, **ISUP:** international society of urological pathology; **PSA:** prostate specific antigen; **WHR:** Waist to Hip Ratio.*

Figure 1. Schematic representation of the study design (a). Summary of the patients' baseline characteristics for the whole cohort and stratified by treatment arm (b).

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A NOVEL ANATOMICAL ROBUST OPTIMIZATION STRATEGY TO ACCOUNT FOR VARIATION IN BLADDER AND RECTUM FILLING AND PTV LOCATION DURING VMAT-IMRT TREATMENT FOR PROSTATE CANCER: A RADIOSA TRIAL (AIRC IG-22159) SPIN-OFF STUDY

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Aims: Anatomical variation in SBRT treatments can have a major impact both on target coverage and OARs sparing due to steep dose gradients. Classical optimization used in the planning process considers uncertainties in patient setup, neglecting anatomical inter-fraction variations. Aim of the present study, side project of the phase II randomized clinical trial RADIOSA (AIRC IG-22159), is to develop and test a novel optimization method accounting for inter-fractional variations in the treatment of oligometastatic prostate cancer (PCa).

Methods: Five oligometastatic PCa patients (pts) with lymph node localizations enrolled within the RADIOSA trial, treated with SBRT at our Institution between 2021 and 2022 with PTV close to bladder and rectum. Traditionally optimized plans were generated in the nominal scenario (planning-CT) using 5 mm as PTV margin. Robust multipleCT-plans were created by including 5 additional synthetic CTs - 1 simulating the expansion of bladder and rectum (defined according to a previous analysis on pts enrolled in the same trial) and 4 simulating PTV displacement by 5 mm in anterior, posterior, superior and inferior direction – and using 3 mm as PTV margin. Both plans simulated a 30Gy/3fx VMAT treatment optimized in Raystation v11.0 according to Timmerman constraints and calculated with CCC algorithm were tested with robust evaluation, simulating a 0.3 mm shift of the patient in all the directions for a total of 6 scenarios. Variations between nominal and worst scenario in dosimetric parameters and homogeneity index (HI) were collected for target coverage and OARs to compare the two strategies.

Results: Overall, the novel optimization method showed smaller variations between nominal and worst-scenario compared to the traditional one. In particular, the major advantage in terms of plan robustness was registered for D98 (-2.31%) and HI (-8.27%), for target coverage and and rectum D0 (-6.48%), as reported in Table1; rectum D1 and D2 showed a slightly greater variation (D1: +0.92%; D2: +0.23%), however, this had no impact on planning objectives.

Conclusion: These preliminary data suggest that inclusion of synthetic CTs accounting for patient anatomy variations in the optimization process results in more robust plans that can meet clinical goals despite a smaller CTV margin. Further perspectives foreseen the inclusion of additional patients to obtain more robust data. This could potentially allow for future dose escalation approaches.

Table 1. Summary of the median absolute percentage variations between worst and nominal scenario for traditional (ΔT column) and MultipleCT plans (ΔM column) and the relative difference (last column).

	$\Delta T = W_T - N_T$ (%)	$\Delta M = W_M - N_M$ (%)	$\Delta = \Delta M - \Delta T$ (%)
PTV			
D98	5.41	3.09	**-2.31**
D50	0.58	0.45	-0.13
D1	0.35	0.32	-0.03
HI	14.58	6.32	**-8.27**
Bladder			
D0	9.51	8.68	-0.83
D1	15.91	14.86	-1.04
D2	15.90	14.48	-1.42
Rectum			
D0	26.50	20.02	-6.48
D1	18.23	19.15	+0.92
D2	18.07	18.30	+0.23

List of abbreviations: W_T (traditional plan, worst scenario); N_T (traditional plan, nominal scenario); WM (MultipleCT Plan, worst scenario); NM (MultipleC$_T$ Plan, nominal scenario); PTV (Planning Target Volume).

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REIRRADIATION OF LOCALLY RECURRENT PROSTATE CANCER WITH CYBERKNIFE® SYSTEM OR VOLUMETRIC MODULATED ARC THERAPY (VMAT) AND IGRT-CLARITY® : OUTCOMES, TOXICITIES AND DOSIMETRIC EVALUATION

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Aims: The management of prostate cancer recurrence following external beam radiotherapy is not defined yet. Stereotaxic body re-irradiation therapy, showed encouraging results for local and biochemical control. Aim of our study was to compare the prostate cancer re-irradiation performed by stereotactic ablative radiotherapy with

Cyberknife® *vs* VMAT/IGRT-Clarity®, relating urinary and rectal toxicities and biochemical control. Further, rival plans achieved by the two techniques were dosimetrically compared.

Methods: From April 2017 to December 2020, 29 patients with prostate cancer recurrence were collected, joining the retrospective studies CyPro (prot. 46/19 OSS) and CLARO (Prot.19/20 OSS) trials. Patients received Cyberknife® treatment (17pts) or alternatively VMAT (Volumetric Modulated Arc Technique) therapy by IGRT (Image-Guided Radiation Therapy)/Clarity® (12pts).

Results: By comparing the re-irradiation of two groups, urinary (GU), rectal (GI) toxicities and biochemical control were investigated. Further, the two techniques were dosimetrically compared by rival plans. The VMAT-IGRT Clarity® treatments were replanned with an optimized template developed for prostate VMAT-SBRT in FFF mode keeping the same dose and fractionation scheduled for Cyberknife Group (30 Gy in 5fx, at 80% isodose). In the CK group twentythree % of patients experienced grade 2 acute GU, while six% grade 2 acute GI. In the VMAT-Clarity® group, acute GU toxicity was recorded in seventeen %, while for eight % grade 2 late toxicity was recorded.

Conclusions: The dosimetric analysis shows that the VMAT-FFF allow to deliver a biological equivalent dose to CK, with the advantage of reducing the likelihood of toxicities arise.

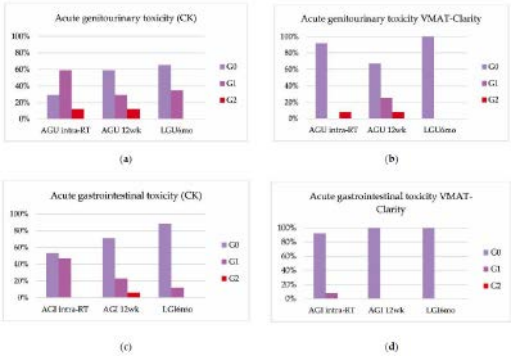

Figure 1.

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ULTRA-HYPOFRACTIONATED RADIOTHERAPY IN PROSTATE CANCER: TOLERANCE AND QUALITY OF LIFE

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Aims: Ultra-hypofractionated radiotherapy (UHRT) has become a valid option for the treatment of localized prostate cancer. In randomized trial, it was found not inferior to conventionally fractionated external beam radiotherapy. This study aims to evaluate acute, late toxicity and quality of life (QoL) during and after UHRT in low and intermediate-risk prostate cancer patients.

Methods: All consecutive patients from 2018 to 2021 with diagnosis of localized prostate cancer were included. All patients were over 70 years-old and with good urinary function, assessed by International Prostate Symptom Score (IPSS) questionnaire and uroflowmetry. Patients received 35 Gy in 5 fractions one day on and one day off with VMAT technique and daily-IGRT with cone-beam CT. Acute and late toxicities were assessed according to CTCAE vs 5 and administration of IPSS score questionnaire first, at the end of the treatment and then every six months.

Results: The study included 33 prostate cancer patients (71–83 years, median 77) with clinical stage T1-T2 N0 M0, median combined Gleason score of 6 (3–8), and median PSA of 10 ng/mL (4–20 ng/mL). Neoadjuvant androgen deprivation therapy (ADT) was given to 12 patients (36.3%) and stopped in 9 patients (27.3%) and in 3 patients (9%) after 6 months and 12 months, respectively. Median follow-up was 30 months (12–42). Median nadir PSA level was 0.03 ng/mL for all patients and 0.6 ng/mL for patients without ADT. No patients had PSA failure. There were no acute grade III and IV toxicities. 11 patients (33%) had grade II acute bladder toxicity and 5 patients (15%) had grade II acute rectal toxicity. No grade III or IV late gastrointestinal or genitourinary toxicities were reported. Grade II late urinary symptoms were observed in 3 patients (9%) and gastrointestinal symptoms in 3 patients (6%). QoL was very good and improved during the observational period.

Conclusions: Despite a small number of patients, this study shows that UHRT in localized prostate cancer is safe and well tolerated treatment with adequate patient selection and particular attention to set-up, planning and delivery. However, a long-term follow-up is necessary to better evaluate outcomes and late toxicities.

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ACUTE AND LATE TOXICITY OF ULTRA-HYPOFRACTIONATED RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER: VMAT VS HELICAL TOMOTHERAPY. A MONOISTITUTIONAL EXPERIENCE

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Purpose: To evaluate the incidence of acute and late toxicity after ultra-hypofractionated radiotherapy using Linac Volumetric Modulated Arc Therapy (VMAT) compared with helical Tomotherapy (TOMO).

Methods: From October 2018 to December 2021, 61 consecutive patients with localized prostate cancer (cT1-

2, GS< 8, PSA<20 ng/ml) were randomized to Linac VMAT and to helical Tomotherapy. 32 patients (52.5%) were treated with Linac VMAT and 29 (47.5%) with TOMO. Patients were monitored before therapy, weekly during therapy, 2 weeks, three, six and twelve months after radiotherapy was completed, using RTOG GI and genitourinary toxicity grading scale. Patients received radiotherapy schedule according to histology reports following international guidelines. Doses were prescribed to planning target volumes (PTV) as the followings: 36.25 Gy (7.25 Gy/fx) to in 5 fractions, 30 Gy (6 Gy/fx) to in 5 fractions and 35 Gy (7 Gy/fx) to in 5 fractions. Dose to abdominal cavity, both femoral heads, bladder and rectum were constrained below each tissue tolerance.

Results: Median age of the patients was 70.5 (range 53-83 years). At the end of the treatment, 1/29 patients (3.4%) in the TOMO group vs. 5/32 (15%) patients in the Linac VMAT group had G1 grade of GI toxicity (p=0.009), while 0/29 (0%) patients in the TOMO group vs. 3/32 (8%) patients in the Linac VMAT group had G2-G3 grade of GI toxicity. 12/29 (40.2%) patients in the TOMO group vs. 17/32 (51.8%) patients in the Linac VMAT group had G1-G2 grade of GU toxicity (p=0.04), while 0/29 (0%) patients in the TOMO group vs. 1/32 (3.1%) patients in the Linac VMAT group had G3 grade of GU toxicity. No G4 grade of GI and GU toxicity was showed. After 12 months from the end of the treatment, 0/29 (0%) patients in the TOMO group vs. 2/32 (6%) patients in the Linac VMAT group had G1-G2 grade of GI toxicity, while 3/29 (10.3%) patients in the TOMO group vs. 6/32 (18%) patients in the Linac VMAT group had G3 grade of GU toxicity.

Conclusions: Acute toxicity is very low. Most of the recorded symptoms decrease over time. A small increase in mild toxicity, statistically significant, was observed in the Linac VMAT group when compared with TOMO group. Our study confirmed that Tomotherapy allows for safe Ultra-hypofractionation, offering a shorter overall treatment time, a lower rate of acute and late toxicities and providing potentially more economic health care.

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STEREOTACTIC BODY RADIOTHERAPY IN THE TREATMENT OF LOCALIZED PROSTATE CANCER: TOXICITY PROFILE ANALYSIS AND TECHNICAL COMPARISON BETWEEN RADIOTHERAPY CENTRES IN CAMPANIA

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Aims: Moderate hypofractionation has been shown to be non-inferior to conventional fractionation in localized prostate cancer (LPCa). Stereotactic body radiotherapy (SBRT) represents an extreme form of hypofractionation, which has proven to be safety and efficacy in this setting of patients (pts), allowing shorter treatment courses. The AIRO Campania regional society performed a retrospective evaluation among patients with LPCa treated by different SBRT techniques.

Method: We collected clinical and technical radiotherapy parameters of LPCa pts undergoing SBRT from January 2019 to April 2022. Toxicity profile and biochemical relapse free survival (bRFS) have been evaluated.

Results: 124 patients from 4 different centers have been included in the present analysis (68 pts low-, 30 pts favorable intermediate-, 18 pts unfavorable intermediate, 6 pts high- and 2 very high-risk cases). All pts received SBRT performed with Cyber-Knife®-system (CK) in 24 pts, Helical Tomotherapy (HT) in 26 pts, Volumetric Modulated Arc Radiotherapy (VMAT) with Clarity ultrasound system in 36 pts and VMAT in 38 pts. Median prescription dose was 35Gy (range 25 – 36.25) in 5 fractions with a median dose per fractions of 7Gy (range 5 – 7,25). Target volume was prostate in 71 pts and prostate plus seminal vesicles in 53 pts. 40.6% of pts received hormone therapy. All pts completed SBRT without interruptions. Genitourinary (GU) acute and subacute toxicity was graded as G0 in 70 pts (56.5%), G1 in 33 pts (26.6%), G2 in 20 pts (16.1%) and G3 in 1 pt (0.8%). Gastrointestinal (GI) acute and subacute toxicity was graded as G0 in 88 pts (70.9%), G1 in 22 pts (17.7%), G2 in 13 pts (10.5%) and G3 in 1 pt (0.8%). There was no G4 toxicity. 14 pts developed a G1 GU late toxicity while 18 pts a G1 GI late toxicity. All pts performed clinical evaluation every 3 months. Overall, 1-year biochemical relapse-free survival (bRFS) was 97.6%.

Conclusions: Despite its retrospective nature, our analysis of 124 treated with SBRT reported a safe mild toxicity profile; only 2 pts developed grade 3 acute toxicity, one pt gastrointestinal while the other one genitourinary. Indeed, a longer follow-up is needed to assess the late toxicity profile, as well as long-term bRFS.

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INFLUENCE OF PATIENT SET-UP AND ORGAN MOTION ON CTV TO PTV MARGINS FOR VMAT MODERATELY HYPOFRACTIONATED RADIOTHERAPY IN PROSTATE CANCER: A RETROSPECTIVE PRELIMINARY ANALYSIS OF 161 CBCT IMAGES IN 7 CONSECUTIVE PATIENTS

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Aims: The aim of the present investigation was to evaluate the influence of inter- and intra-fraction set-up error and prostate motion on CTV–PTV margins in patients (pts) receiving VMAT radical moderately hypofractionated radiotherapy (VMHRT) for prostate cancer.

Method: 161 CBCT images from 7 pts with Low (LR)/Medium (MR) Risk (NCCN) prostate cancer radically irradiated with VMHRT were retrospectively analyzed. All pts were treated with full bladder and empty rectum (enema and specific diet). CTV was defined as prostate only (P) for LR and prostate + insertion of seminal vesicles (PSV) for MR pts, without elective nodal irradiation; PTV was defined as CTV + 9 mm isometric; prescription dose to PTV (ICRU 83) was 70 Gy in 2.5 Gy daily fractions. A pre- and post-treatment CBCT was acquired in all pts during the first 10 days (to account for both inter- and intra-fraction error) and then pre-treatment CBCT only was acquired once a week to monitor inter-fraction set-up error. CTV was re-contoured on each CBCT by the same radiation oncologist to eliminate inter-observer variability. 91 CBCT before RT and 70 CBCT after RT were analyzed. Inter-fraction errors were calculated by statistical analysis of shifts in bony anatomy (B), shift in CTV position (T) and considering the Prostate Motion (PM), derived from the mathematical difference between T and B, comparing pre-treatment CBCT with CT simulation scan. The intra-fraction error was calculated comparing pre-treatment CBCT with post-treatment CBCT. The van Herk formula (PTV margin=2.5Σ+0.7Σ) was applied to calculate PTV margins of P/PSV using CBCT. The non-IGRT margins were calculated considering both inter- and intra-fraction motion uncertainties; while the margins for IGRT scenarios were calculated on the basis of intra-fraction PM data alone.

Results: The magnitudes of vector shift of inter-fraction B and PM are respectively 2.4 mm and 1.7 mm, while the magnitudes of intra-fraction are 0.4 mm and 1 mm. Using the Van Herk formula and inter- and intra-fraction motion data, the CTV-PTV margins with IGRT are 3.4 mm (AP), 3.5 mm (SI) and 1 mm (LL) and without IGRT are 8.5 mm (AP), 5.4 mm (SI) and 5.3 mm (LL).

Conclusions: Based on our preliminary results, daily IGRT will ensure 95% of the prescribed dose will be delivered to the CTV in 90% of patients (Van Herk formula) with margins CTV-PTV of 3.5 mm in AP and SI and 1 mm in LL.

P228

ACUTE AND LATE TOXICITIES IN LOCALIZED PROSTATE CANCER PATIENTS TREATED WITH MODERATE HYPOFRACTIONATED DEFINITIVE RADIOTHERAPY DELIVERED BY VOLUMETRIC MODULATED ARC THERAPY (VMAT): PRELIMINARY ANALYSIS OF OUR RETROSPECTIVE EXPERIENCE

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Aims: The aim of this study was to evaluate acute and chronic genitourinary (GU) and gastrointestinal (GI) toxicities in patients treated with pelvic volumetric modulated arc therapy (VMAT) radiotherapy for localized prostate adenocarcinoma.

Methods: We retrospectively analyzed 141 consecutive patients treated between July 2012 and December 2021 in Our Institution. All of them underwent VMAT definitive Radiotherapy applying moderate hypofractionation on the prostate (70,2 Gy in 26 fractions at 2,7 Gy/fraction). The median age at the time of treatment was 72 years (range 65-82 years). Gleason Score was 6 (3+3) in 38 pts (27 %) and 7 (3+4 or 4+3) in 73 pts (52%) and >/= 8 in 30 pts (21%). Median initial PSA was 10,8 ng/mL and ADT was administered in 116 (82%) patients. Prescription dose was 95% of PTV to be covered by at least 95% of the prescription dose. Patients were treated with full bladder and empty rectum, according to international prostate guidelines. CBCT daily images were taken for entire duration of treatment, applying set-up corrections whenever needed. The Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 was adopted for toxicity evaluations. Acute toxicities were assessed through a clinical visit at a median time of 60 days from last day of treatment, while late toxicities were assessed at a median time of 24 months from the date of treatment.

Results: All patients were treated with a scheduling of 270 cGy / 26 fractions. The Target Volume involved prostate and seminal vescicles area and all patients completed the planned treatment. After a median follow-up of 27 months (range 6-48 months), we recorded 73 patients with acute GU toxicities: in particular, G1 65 patients (88%), G2 4 patients (6%), G3 4 patients (6%) and none G4 events. For Acute GI toxicities were reported by 37 patients, of which: G1 in 29 patients (78%), G2 in 5 patients (13%) and G3 in 3 patients (9%). Only 1 patient developed chronic G1 GU toxicity, among which cystitis. Chronic GI toxicities were reported by 4 patients: G1 3 patients with proctite (75%), G2 only 1 pts with rectorrhagia (25%) and no G3-G4 late toxicities.

Conclusions: Our analysis confirms the excellent tolerability and low incidence of acute and late toxicity of

VMAT treatments delivered to prostate with a moderate hypofractionation. These results are consistent with published current data in this setting.

P229

INTER-OBSERVATOR COMPARISON STUDY AMONG RADIOTHERAPISTS IN THE ASSESSMENT OF DAILY CBCT FOR IGRT IN PATIENTS TREATED FOR PROSTATIC CANCER WITH OR WITHOUT INTRAPROSTATIC FIDUCIALS

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Aims: Modern advanced radiotherapy treatments of prostate cancer are usually associated to daily positioning verification systems to correct possible random errors and target displacement. The cone beam computed thomography (CBCT) is the most commonly used system. It may or may not be associated with the positioning of intraprostatic radiopaque fiducials. We wanted to investigate the possible advantage of using intraprostatic markers in daily repositioning via CBCT.

Method: In our center, the patients treated for prostate cancer undergo daily CBCT, and the treatment includes two possible schemes, 20 or 28 daily sessions (5 fractions per week). Three CBCT exams were selected for each treatment course, concerning the first, last, and the median (eleventh or fifteenth session according to the scheme used). Thirteen patients were identified, and 39 exams selected. Six patients (46%) had no intraprostatic implanted markers, while 7 (54%) had them. Seven Radiation Oncologists, with at least seven years of experience in CBCT evaluation, retrospectively reviewed the selected 39 exams, recording the movements of the treatment table to reposition the patient in the correct position with respect to the planning CT, and the time consumed to do it, to identify possible differences in the two groups of patients. Analysis of variance was carried out for comparison of different groups and *t*-test for unpaired data was used to test difference in mean values of different parameters related to movements ($p<0.05$ was set as significance level – analysis was made with Microsoft Excel 2013).

Results: No statistically significant difference was found between operators nor in the analysis of image with fiducial markers neither in images without them. A difference between the two groups of patients was only found in the mean values of angle correction, higher in the fiducials group (Y° - p=0.04 and Z° - p=0.01), and in mean time for image analysis, shorter in the same group (p=0.03).

Conclusions: According to our study, the use of intraprostatic seed markers, added to daily CBCT, seems usefull to better detect the presence of rotation errors allowing their correction. Furthermore, it reduce time to treatment start, very important to reduce the risk of intrafraction organ motion and target missing.

P230

A COMPARISON OF CLINICAL OUTCOMES BETWEEN THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY AND INTENSITY-MODULATED RADIOTHERAPY IN THE ADJUVANT SETTING OF PROSTATE CANCER: A CASE-CONTROL STUDY

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Aims: Aim of this study was to evaluate clinical outcomes after three-dimensional conformal radiotherapy (3D-CRT) versus intensity-modulated radiotherapy (IMRT) in two cohorts of patients treated with radical prostatectomy and adjuvant radiotherapy (RT). Primary endpoint was to compare the toxicity rates related to the two RT techniques.

Method: We collected data from 226 patients who underwent adjuvant RT (50% treated by 3D-CRT, 50% by IMRT) after radical prostatectomy. The two patients' cohorts were matched according to pelvic nodal RT and hormonal therapy. The main tumor and treatment characteristics are shown in Table 1. We scored and compared both acute and late gastrointestinal (GI) and genitourinary (GU) toxicity based on the RTOG criteria. The comparisons between the two cohorts were calculated by Chi-square and log-rank test for acute and late toxicity, respectively. This analysis is part of a multicenter observational study (ICAROS trial) approved by the ethics committees of the participating centers.

Results: A total of 226 patients with a median age of 67 years (range: 43-81) were included in this study. Patients were treated with a median total dose of 70 Gy and the median follow-up was 51.5 months. Patients treated with IMRT experienced higher acute toxicity rates (GI: 15.9% vs 9.7%; p: 0.164; GU: 23.0% vs 8.8%; p: 0.04), but lower ten-year G3 late toxicity-free survival (GI: 100% vs 94.2%; p: 0.120; GU: 92.8% vs 83.5%; p:

0.057). No significant differences were observed in terms of overall survival and biochemical and local control between the two treatment groups.

Conclusions: Both techniques resulted in comparable control of the disease. IMRT was associated with lower G3 late GI/GU toxicity, with a trend towards statistical significance. However, surprisingly enough, acute toxicity rates were significantly higher compared to 3D-CRT.

Table 1. Patients and treatment characteristics and acute toxicity results.

Variable	Value	Total (%)	3D-CRT (%)	IMRT (%)
Age at diagnosis (years)	Median (range)	67 (43-81)	66 (50-81)	68 (43-81)
iPSA (ng/ml)	Median (range)	8.2 (0.4-127.0)	9.9 (1-127)	7.6 (0.4-83.0)
pT	1 (1a-1b)	1 (0.4)	0 (0)	1 (0.9)
	2	58 (25.7)	26 (23.0)	32 (28.3)
	3 (3a-3b)	165 (73.0)	87 (77.0)	78 (69)
	4	1 (0.4)	0 (0)	1 (0.9)
pN	N0	126 (55.8)	57 (50.4)	69 (61.1)
	N1	21 (9.3)	7 (6.2)	14 (12.4)
ISUP	1	50 (22.1)	38 (33.6)	12 (10.6)
	2	38 (16.8)	15 (13.3)	23 (20.4)
	3	58 (25.7)	34 (30.1)	24 (21.2)
	4	41 (18.1)	16 (14.2)	25 (22.1)
	5	39 (17.3)	10 (8.8)	29 (25.7)
Total dose (Gy)	Median (range)	70.0 (60.0-73.8)	70 .0 (60.0-73.8)	66.0 (60.0-73.8)
Pelvic nodal irradiation	No	123 (54.4)	62 (54.9)	61 (54.0)
	Yes	103 (45.6)	51 (45.1)	52 (46.0)
Hormonal therapy	No	137 (60.6)	71 (62.8)	66 (58.4)
	Yes	87 (38.5)	42 (37.2)	45 (39.8)
Acute GI toxicity	G≤1	197 (87.2)	102 (90.3)	95 (84.1)
	G≥2	29 (12.8)	11 (9.7)	18 (15.9)
Acute GU toxicity	G≤1	190 (84.1)	103 (91.2)	87 (77.0)
	G≥2	36 (15.9)	10 (8.8)	26 (23.0)
Follow-up (months)	Median (range)	51.5 (2-240)	84.0 (6-240)	37.0 (2-143)

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ABSTRACT NOT PUBLISHABLE

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STEREOTACTIC BODY RADIOTHERAPY TO LYMPH NODE IN OLIGOMETASTATIC PROSTATE CANCER

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Purpose: The purpose of the study was to evaluate the efficacy, safety and toxicity of extracranial stereotactic body radiotherapy (SBRT) for lymph node oligometastatic/recurrent/persistent prostate cancer (PCa).

Material/Methods: Patients included in this analysis had < 3 metastatic sites and underwent SBRT on nodal metastases. The endpoints were local control of treated metastases (LC), distant local control (DLC), progression-free survival (PFS), overall survival (OS), distant metastases free survival (DMFS). Acute and delayed toxicities were also evaluated.

Results: Thirty-nine patients carrying out 62 nodal metastases were analyzed. In 16 patients androgen deprivation (AD) was combined with SBRT. Fifty-three lesions (85.4%) were treated by SBRT (multiple fractions), and 9 (14.2%) lesions were treated by single fraction radiotherapy (SRS). The median dose delivered by SBRT was 45 Gy (range 24-50 Gy) with a median BEDα/β10 of 48 Gy (range 45-95.2 Gy). The most frequent schedula for SBRT was 6 Gy x 5 fractions (46%). The median dose delivered by SRS was 12 Gy (range 8-30 Gy), with a median BEDα/β10 of 71.4 Gy (range 33.6-120). The most frequently adopted schedule for SRS was 12 Gy x 1 fraction (33.3%). The median follow-up was 30 months (range 5 – 116). The LC rate at three and five years was 98% and 93.5%, respectively. The observed median of DNC was 28 months with a five-year rate of 81.9% The median PFS was 12 months; the three-year PFS rate was 33.9%. The median DMFS was 28 months; the five-year DMFS rate was 56.9%. Median OS was 30 months. No grade III or IV toxicity was reported.

Conclusion: The present study shows the efficacy of SBRT in oligometastatic/persistent/recurrent prostate cancer patients and is able to achieve good results in terms of clinical outcomes with poor toxicity.

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EVALUATION OF NODAL SABRT IN OLIGORECURRENT CSPC PATIENTS

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Aims: Today recent advance in imaging techniques like using fluorocholine (FCH) PET/CT or prostate-specific membrane antigen (PSMA) PET/CT, allowed to early detect oligorecurrent prostate cancer patients. Oligorecurrent pelvic nodal relapse in prostatic cancer is a challenge for regional salvage treatments, and the role of radiotherapy in the management of these patients could delay the start of Androgen Deprivation Therapy (ADT). The aim of this study is to evaluate biochemical progression free survival time (bPFS) in nodal oligorecurred patients in order to delay ADT start.

Methods: This is a retrospective observational study conducted in our center, including nodal oligorecurred prostate cancer patients, treated at our hospital with stereotactic radiation therapy (SABR/SBRT). At time of biochemical failure after primary treatment, all patients underwent to 18FCh-PET/CT or PSMA PET/CT, and those with nodal oligorecurrence were treated with a VMAT technique and daily pre-treatement ConeBeam Computed Tomography (CBCT), with a BED3>100 Gy. Time to bPFS was than recorded and evaluated according to pre-SABR PSA doubling time (PSA-DT) and ISUP.

Results: Between January 2018 and March 2022, 24 nodal oligorecurred patients were treated with SABR, with median time to bPFS of 42.5 months and 3 years bPFS of 60.6% (Figure 1). No differences were observed

according to PSA-DT (greater or less of 6 months) (Figure 2), or ISUP class (greater or less of 3) (Figure 3).

Conclusions: These results underline the potential role of SABR in delaying ADT treatment in nodal oligo-recurrent CSPC patients.

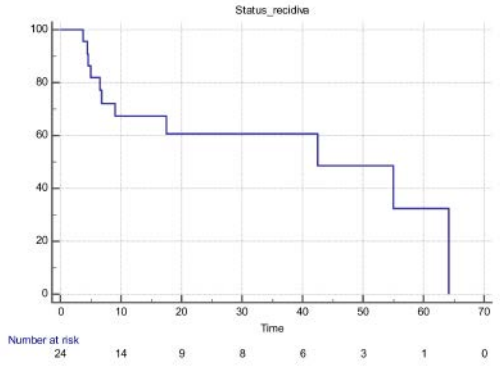

Figure 1. Biochemical progression free survival time (bPFS) in nodal oligorecurred patients: median time to bPFS of 42.5 months and 3 years bPFS of 60.6%.

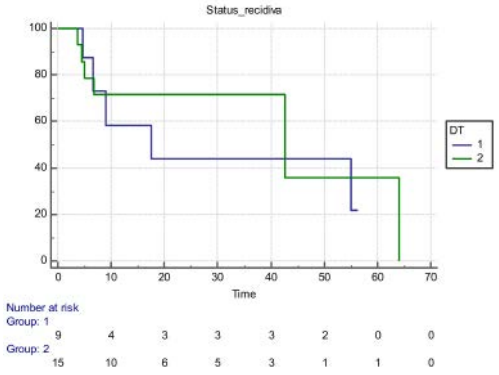

Figure 2. bPFS according to PSA-DT: no differences were observed according to PSA-DT greater (2) or less (1) of 6 months) [p=0.6].

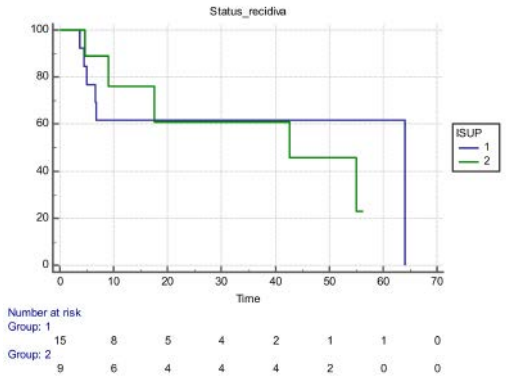

Figure 3. bPFS according to ISUP class: no differences were observed according to ISUP class greater (2) or less of 3 (1) [p=0.9].

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OMITTING ELECTIVE PELVIC NODES IRRADIATION IN HIGH RISK PROSTATE CANCER: REPORT ON 33 CONSECUTIVE PATIENTS

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Aims: Radiotherapy coupled with androgen deprivation therapy (ADT) is one of the treatment options for both localized and locally advanced high risk prostate cancer (PC). The benefit of prophylactic irradiation of pelvic lymph nodes, in the absence of regional pelvic nodal involvement, is still a matter of debate. In this report we present the data about consecutive patients treated irradiating the prostate target without draining nodes in our institution.

Method: From September 2016 to January 2021 a total of 33 patients classified as high or very high risk PC according to 2020 NCCN Risk Group stratification were treated. Median age at diagnosis was 75 year (60-82); all patients were staged with abdominal MRI or CT and bone scan. Ten patients underwent also either 68Ga-PSMA PET/CT or 18F-Choline PET/CT. All resulted clinically N0, cT3-cT4 and/or ISUP Grade Group 4-5 and/or PSA serum levels at diagnosis >20 ng/ml. Androgen suppression using gonadotropins hormone-releasing analogs before, during and after RT, for a minimum period of 6 months to a maximum of 3 years was administered. Except for one patient treated with SBRT (42.7 Gy in 7 fx) and one patient treated with conventionally fractionated EBRT (76 Gy in 38 fx), all patients were treated with moderately hypofractionated radiation therapy (66.7-70 Gy in 25-28 fx) on the prostate. Biochemical failure was defined as a serum PSA exceeding nadir PSA + 2 ng/ml; for the Metastasis-Free Survival (MFS) assessment it was considered the cancer spread in any other parts of the body. Biochemical Failure-Free Survival (BFFS), MFS and Overall Survival (OS) were calculated from the time of diagnosis.

Results: At a median follow up of 35 months (15-67), 1 biochemical failure was observed, with corresponding estimated 3-year and 5-year BFFS of 100% (Figure 1B); 3-year and 5-year MFS of 100% (Figure 1B) with only one patient experiencing metastatic disease after 65 months of follow up. The number of deaths for any cause observed was 3, with corresponding 3-year and 5-year OS of 100% and 84.8%, respectively (Figure 1C).

Conclusions: Our data suggest that omission of pelvic irradiation in patients with high risk localized prostate cancer may be not deleterious for disease control. A study

with a better numerosity and a longer follow up is mandatory to confirm this suggestion.

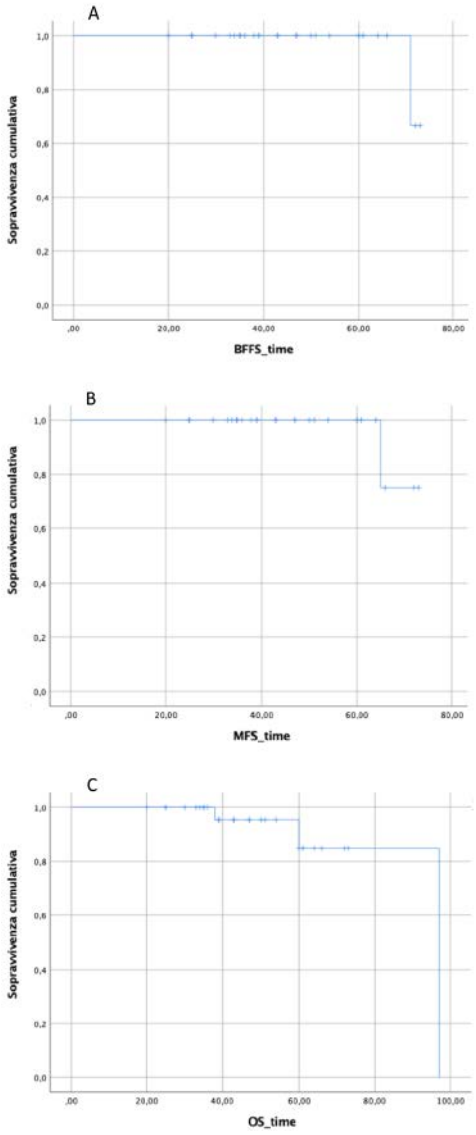

Figure 1. Kaplan-Meier estimates of (A) biochemical failure-free survival, (B) metastases free-survival, (C) overall survival.

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RADIOTHERAPY IN PEDIATRIC SARCOMAS OF THE PROSTATE: TWO CASE REPORTS

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Prostate sarcomas are rare childhood tumors whose survival has changed significantly thanks to multimodal therapies. We describe our experience with two pediatric case, both treated with VMAT radiotherapy. The first patient is a 14 years old boy affected by metastatic embryonic rhabdomyosarcoma of the prostate. He started EPSSG-RMS 2005 chemotherapy protocol. After 6 months, he received a concomitant RT. 5 mm TC simulation with Vac-Lok Cushion was performed, in supine position with empty rectum and full bladder. GTV1 was identified as tumor volume and pathological pelvic lymph nodes, CTV1 as GTV1 + 1cm, PTV1 as CTV1+ 0,5 cm, PTV2 as CTV1 excluding inguinal lymph nodes and PTV3 as post-CHT residual disease. A daily dose of 180 Gy (total dose 5580 cGy in 31 fractions) with a sequential scheme of 4140 cGy to PTV1, 900 cGy as boost to PTV2 and 540 cGy as overboost to PTV3 was given. After 3 months, to treat the lung metastases, a total lungs irradiation was delivered: 150 cGy/fr in 10 fr (total dose 1500 cGy). After 1,5 year, because of a residual prostatic nodule he underwent TURP and a Stereotactic Body RT only on the prostate with a dose of 7 Gy in 5 fr (total dose 35 Gy). RMN showed stable metastatic lesions and persistence of prostatic disease, hence he underwent radical prostatectomy and CHT. The second patient 2 is a 4 years old boy affected by rhabdoid tumor of the prostate. RMN showed a nodule in the right lobe and pelvic lymphadenopathies. He started the same chemotherapy protocol. After 3 cycles, RMN showed no progression and he started RT. TC simulation was performed with the same setting. CTV1 was identified as entire prostate and bladder base, CTV2 as the nodule in the prostatic right lobe and PTV as CTV1 + 3 mm. We used a Simultaneous Integrated Boost (SIB) scheme in 30 fr of 180 cGy on PTV and 199 cGy/fr on CTV2 (total doses 5400 cGy and 5890 cGy). Both patients well tolerated the pelvic RT without acute urinary toxicity. At the last follow up, only the first one presented recurrent cystitis and low-grade urinary incontinence but no toxicity related to TLI. TC-PET showed no more lung and bone progression. The second patient's last RMN showed an halved lesion compared to previous imaging. Currently, they're still in follow up. Because of the poor number of cases, our experience is yet limited. Future recruitment of patients will allow to collect more treatment's outcome data for a best evaluation of RT's tolerance and efficacy.

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MONITORING OF URINARY FUNCTION IN PATIENTS WITH PROSTATIC CANCER UNDERGOING MODERATE HYPOFRACTIONATED RADIOTHERAPY TREATMENT WITH VMAT TECHNIQUE

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Aims: Evaluate the impact of moderate hypofractionated moderate radiotherapy for localized prostatic cancer on acute and late urinary toxicity using the urodynamic examination and the International Prostatic Symptoms Score (IPSS) questionnaire.

Method: Between June 2019 and April 2022 patients with localized prostatic cancer underwent Volumetric Modulated Arc Therapy (VMAT) conventionally fractionated (78 Gy/39 fractions) or moderate Hypofractionated radiotherapy (73,5Gy/30 fractions or 70Gy/28 fractions). All of them underwent urodynamic tests (uroflowmetry) and the IPSS questionnaire before starting the radiotherapy treatment, in the middle and at the end of the treatment and then every 6 months during the follow-up.

Results: Of 210 patients, 180 were evaluable. All of them underwent a rectal and bladder preparation protocol (empty rectum and comfortably full bladder). 150 pazients underwent conventional fractionation, 30 patients underwent a moderate hypofractionated radiotherapy. Daily image guided radiotherapy (IGRT) setup was performed by Cone beam CT and assessed the adequacy of the patient's preparation and positioning. IPSS basal score greater than 15 as well as urinary flow less than 4 ml/sec were considered exclusion criteria for moderate hypofractionated treatment. A more rapid but not significant worsening of the IPSS score and urinary flow was observed during treatment in the group of patients undergoing moderate hypofractionation compared to conventional fractionation. No significant differences were found in OAR DVHs between patients. No grade 3/4 toxicities were reported.

Conclusions: IPSS and urinary function tests are a valid tools for an objective evaluation of urinary toxicity related to radiotherapy treatment. VMAT technique with daily IGRT Cone beam CT and patient preparation ensure a good tolerance profile of radiotherapy treatment in both conventional and moderate hypofractionated fractionation.

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ACUTE AND LATE TOXICITY IN THE COMBINED RADICAL RADIOTHERAPY AND HORMONE THERAPY IN ELDERLY PATIENTS WITH PROSTATE CANCER: A SINGLE CENTER CLINICAL EXPERIENCE

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Aims: The study investigates the onset of acute and late toxicity in patients (pts) with prostate cancer who underwent radical radiotherapy (RT) + androgen deprivation therapy (ADT).

Methods: From January 2017 to January 2021, 40 elderly pts (> 75 years) with prostate cancer with unfavorable intermediate-risk underwent radical radiotherapy in association with ADT. A pre-treatment complete history and clinical evaluation were collected for each pt. All pts underwent cardiological evaluation: glycolipid profile, ECG, and echo pre and post-treatment and every six months. As internal protocol, each patient was screened for osteometabolic risk using bone densitometry and specific serum profile. ADT consisted of an LH-RH agonist or antagonist every month for six months based on the personal cardiovascular profile. RT was started three weeks after the injection. All pts were treated with volumetric modulated arc therapy (VMAT), and the prescription dose was 60 Gy in 20 fractions. The pts were irradiated with an empty rectum and full bladder. Acute and late toxicity were collected using the CTCAE scale (vers. 5).

Results: The median age at the treatment time was 78.4 years (range 75-84 years). The mean follow-up was 23 months (range 16-55). RT was well tolerated: all pts completed the planned treatment without interruptions. All pts are still alive. 9 pts, because of high cardiovascular risk, underwent LH-RH antagonist. 12 pts received vitamin D, calcium supplementation, and denosumab every six months. Hot flashes G1 were observed in 27 pts, G2 in 5 pts. Regarding acute genitourinary (GU) toxicity: 24 pts and 3 pts reported G1 and G2 toxicity, respectively, and no grade 3 or higher toxicity was observed. Late GU toxicity G1-G2 occurred in 4 pts and 2 pts, respectively. Regarding acute gastrointestinal (GI) toxicity: 14 pts developed diarrhea and tenesmus (G1), and 3 pts developed G2 toxicity. No pts developed chronic GI toxicity such as fecal incontinence or rectal stenosis.

Conclusions: Our data suggested that combination RT + ADT was tolerated in elderly patients with a low incidence of GI e GU toxicities.

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PENILE BULB DOSE CONSTRAINTS AND ERECTILE DEFICIENCY RISK IN PROSTATE CANCER PATIENTS UNDERGOING RADIOTHERAPY

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Aims: To find the precise penile bulb constraints dose (anatomically: spongious portion underneath genito-urinary diaphragm) based on dose-volume histograms (DVHs) analisys in patients treated with radiotherapy, and to identify any clinical or anatomic parameters that predicts the risk of Erectile Deficiency. Although neurovascular bundles, the internal pudendal arteries and the corpora cavernosa too contributes to attain and/or maintain erection, these are structures that need MR study to better delineation and contouring. Penile bulb is easily detectable and it seems to be a good surrogate for afore mentioned structures.

Methods: We retrospectively analized datas on n 35° pts with low- and intermediate-risk (3+4) prostate cancer (clinical stage T1c-T2c and iPSA < 20 ug/L) receiving normofractioned radiotherapy from February 2021 to June 2022. Were excluded patients affected by diabetes and hypertension (assuming beta-blocker), assuming PDE5 inhibitor to reduce confounding factors. PB was contoured on each tc slice, without PRV expansion, mean volume 8.2 cm3. The erectile score, at baseline at 1 month from radiotherapy end, was evaluated according to the International Index of Erectile Function questionnaire (IIEF-5).

Results: Median follow-up was 8 months (range 2-16), 85% of patients mantain a good erectile function according to the IIEF-5 (median score: 20 with range of 11–25), during radiotherapy course and in subsequent follow-up programm. A mean dose to the PB was of 30 Gy. The predictive factors of mild erectile decreasing were represented by Prostate (> 40 cc) and PB volume (> 10 cc), probably correlate with tight margin obtained with CTV-PTV expansion.

Conclusions: The close selection patients in the retrospective analysis and the relative exclusion due to vascular, pharmacological and metabolic confounding factors, in order to identify the radiotherapy mainly role in erectile impairment, resulted in a small number of patients. However it indicates, that the threshold dose of PB could be of 30 Gy in order to avoid erectile decline. Further large studies, with more cases and extensive follow-up, are needed for a better and precise Constraints dose definition.

P239

PSA TIME OF NADIR IN HYPOFRACTIONATED EXTERNAL BEAM RADIOTHERAPY FOR PROSTATE CANCER: COMPARISON WITH CONVENTIONAL FRACTIONATION

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Aims: Based on literature data, in conventional external beam radiotherapy for prostate cancer PSA time of nadir is 12 months. The aim of this study is evaluate PSA kinetic in hypofractionated fractionation.

Material and Methods: Between January 2014 and December 2021 a total of 59 patients with prostate cancer were treated with ablative moderate hypofractionated radiotherapy. Six patients were lost in follow up, 53 (90%) patients were evaluated for response and included in this retrospective analysis. Median age was 76 years (range: 56 – 88 years). Histologically 5 patients was in Gleason grade group 1, 11 in GG2, 13 in GG3, 12 in GG4 and 7 in GG5. Pre-treatment PSA was <10 ng/ml in 39 cases, 10-20 ng/ml in 8, >20 ng/ml in 6. Patients were treated with 56 Gy in 16 fractions over 4 weeks. The planning constraints for OAR were rectum V31<40%, V52<10%, V54<3%; bladder V34,3<50%, V52<10%; femoral head Dmax=28Gy, V16,4<50%; penile bulb Dmean=38Gy. Radiotherapy was delivered by 6MV LINAC with VMAT technique, before each fraction isocenter position was verified by CBCT. PSA response was evaluated every 3 months after the end of radiotherapy for 30 months or until disease recurrence. Gastrointestinal and genitourinary toxicities were evaluated contextually according to RTOG/EORTC grading system.

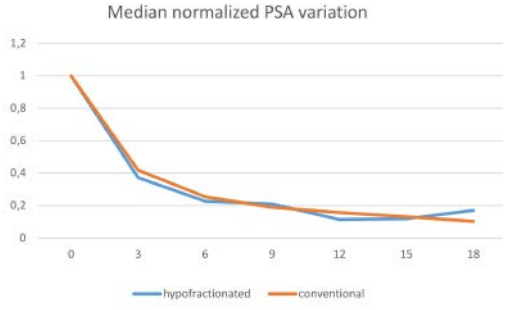

Figure 1.

Results: Median follow up was 13.68 months. PSA time of nadir was 12 months. The results were compared with a control group of patients treated with conventional fractionation (50 Gy to seminal vescicles and 78 Gy to prostate in 2 Gy/fraction daily). Figure 1 reported median normalized PSA variation in hypofractionated and conventional treatmets versus follow up time: PSA kinetic

was analogues in both cases. No relevant differences in toxicity between the two groups was observed, one patient experienced G4 genitourinary toxicity (stenosis) in hypofractionated schedule group. Data analysis were performed in June 2022: during follow up we registred 2 intraprostatic relapses, 2 nodal recurrences and 1 bone metastatis.

Conclusions: Our study suggests that there are no differences between hypofracionated and conventional treatment in term of PSA kinetics, the time of nadir is 12 months in line with literature. No relevant differences in toxicity between the two groups was observed.

P240

HYPOFRACTIONATED RADIOTHERAPY IN PROSTATE CANCER: TOXICITY PROFILES AND SURVIVALS IN OUR INTERNAL CASISTIC

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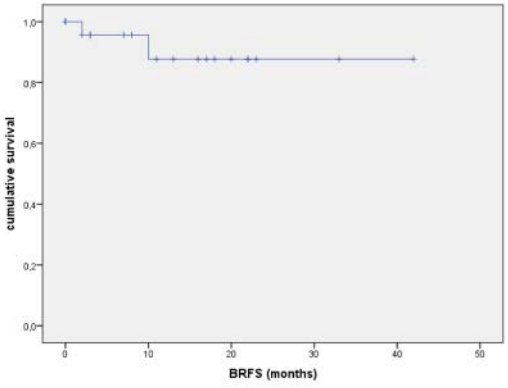
Aims: To analyze acute and chronic toxicity profiles and survival data among patients (pts) with a diagnosis of prostate cancer, treated with hypofractionated radiotherapy.

Methods: Our clinical setting included 26 pts with prostate cancer, treated at our Institute between 2018 and 2022. During follow up, we evaluated genito-urinary, rectal and sexual impairment toxicity data according to CTCAE v5.0. Statistical analysis was performed using SPSS® software.

Results: The median age was 77 years (range 62-85). Karnofsky index was evaluated 1 for 14 pts (54%) and 2 for the remaining. Pts were almost equally distributed among risk categories, with 4 pts (15%), 3 (12%), 2 (8%), 7 (27%), 4 (15%) and 6 (23%) at very low, low, favorable intermediate, unfavorable intermediate, high and very high rank, respectively. Fourteen pts (54%) underwent concomitant ormonotherapy. Radiotherapy was performed with hypofractioned schedule and the prescribed dose to the PTV (the prostatic gland) was 60 Gy/3 Gy per fraction. The treatment was delivered with imaged guide support (Cone-Beam-CT). During treatment an optimal rectum-bladder preparation was strongly recommended. Regarding acute toxicity, 14 pts (54%) did not show any degree of dysuria, while 7 (27%) and 5 (19%) pts reported grade 1 and 2, respectively. Six pts (23%) developed an increase of urinary frequency G1, while 10 (39%) and 10 (39%) showed G0 and G2 events, respectively. Only 3 pts (12%) and 2 pts (8%) developed acute G1 and G2 diarrhea. Twenty-two pts (85%) had no grade of acute proctitis. Regarding chronic toxicity, no pts developed fecal and urinary incontinence. Only 1 pt (4%) developed G2 proctitis and no one rectal stenosis or sexual disfunction. After a median follow up of 7.5 months, 2 pts (8%) developed biochemical relapse (Figure 1); 3 pts (12%) developed metastasis event. At Chi-square analysis, there was a significant correlation (p=0.05 and p=0.01, respectively) between these events and the initial risk category, particularly the pts with an high risk cancer developed disease progression; instead, there was no significant correlation between these events and the association with ormonotherapy. The 2 years overall survival was of 92%.

Conclusions: Our casistic showed low toxicity and good survival data. These data underline that an optimal pts selection, organ motion control and the personalization of treatment delivery are the most important impact factors.

Figure 1.



P241

THE RECTUM IS AN OAR THAT MOVES AND REACTS TO STIMULI DURING PROSTATE CANCER RADIOTHERAPY, HOW CAN IT BE MADE LESS MOBILE?

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Aim: To analyze risk factors for acute and late rectal toxicity during IMRT for prostate cancer. We know from the literature that the position of the rectum at the time of CT treatment planning is probably not fully representative of the position during RT due to inter- or intrafractional variations in rectal filling, intestinal gas, and bladder filling. On the other hand, an empty rectum is recommended during the simulation to avoid introducing a systematic error in the coverage of the PTV. The fact that CT imaging features before and during treatment can predict radiation toxicity and the combination of imaging and clinical / dosimetric features can improve the predictive performance of radiotoxicity modeling. A high rate of acute rectal toxicity is now recognized as being associa-

ted with late RT proctopathy. From these premises we decided to empty the rectum constantly and repeatedly every day from simulation to treatment and then analyze the results.

Patients and Methods: From March 2020 to May 2022. 115 patients received 70-76 Gy in 30-33 fractions in the prostate and seminal vesicles. Each patient was provided with a form explaining how to fill the bladder before treatment and a diet low in fiber and with foods designed to avoid intestinal gas formation was recommended both during the simulation and during the entire treatment. Subsequently, after evaluating the first treated patients, an oral therapy with vegetable charcoal and macrogoal was added. Common Terminology Criteria for Adverse Events version 3.0 was used to classify rectal toxicity. During radiotherapy we measured the displacement of the rectum with respect to the simulation and we evaluated it.

Results: Two groups of patients both on a fiber-free diet but one on a carbon supplement and macrogoal. Acute rectal toxicity occurred in 6 (20.68%) patients (1 grade 3 others G1) in the diet group, in the supplement group in 1 patient (1.16). Measurement of the irradiated rectum during the control cone beam in patients who performed only diet and bladder filling was predictive of the recorded toxicity, in the other group the irradiated rectum was perfectly adherent to the irradiated rectum at the time of the simulation

Conclusion: In prostate cancer patients treated with the IMRT schedule, the use of diet and the supplementation of coal and macro-lens lowered the incidence and degree of acute rectal toxicity better than diet alone. There were no cases of late toxicity in either group.

P242

SYSTEMIC THERAPY-FREE SURVIVAL AS PRIMARY ENDPOINT IN OLIGOMETASTATIC PROSTATE CANCER PATIENTS TREATED WITH METASTASIS DIRECTED THERAPY. A SYSTEMATIC REVIEW

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Aims: After primary curative treatment failure, the best timing concerning the administration of androgen deprivation therapy (ADT) is still debated, at the time of disease recurrence or later. In recent years, the use of functional imaging has been increased, making possible to identify even more oligometastatic patients suitable for stereotactic body radiotherapy (SBRT). A PSA control could be achieved in case all the active lesions are treated, allowing, in selected cases, to postpone the beginning of ADT until than 3/5 synchronous are revealed (therefore, avoiding the onset of side effects due to ADT). The present work aims to make a systematic review of the studies assessing the ADT PFS in the oligometastatic patient treated with SBRT.

Methods: We analyzed papers published on PUBMED using the keywords "prostate cancer", "oligometastasis" "stereotactic body radiotherapy" and we only considered the studies where patients with failure of primary treatment (surgery or exclusive RT with or without irradiation of the pelvis) were subsequently treated with SBRT on metastatic sites of disease without previous or concomitant ADT. Five papers met the inclusion criteria: Berkovic 2013, Bouman-Wammes 2017, Triggiani 2017, Ost 2018 e Pasqualetti 2020; in Triggiani's study we only considered patients not treated with ADT. All studies except Pasqualetti et al had a retrospective design. A total of 220 patients with 314 bone or lymph node metastases were therefore considered.

Results: Berkovic et al enrolled 24 patients with 29 metastases staged with Ch-PET/CT (4) and with FDG-PET/CT (20) and the ADT PFS was 38 months; Boumann-Wammes et al examined 43 patients with 54 metastasis staged with (18 F) FCH PET/TC, the ADT PFS was 15.6 months; Triggiani et al considered 76 patients with 139 metastases staged with Ch-PET/TC and the ADT PFS was 19.1 months; Ost et al analyzed 31 patients with 25 metastases staged with Ch-PET TC and the ADT PFS was 21 months and Pasqualetti et al examined 46 patients with 67 metastases staged with Ch-PET/TC and the ADT PFS was 39.1 months.

Conclusion: Despite the selected studies adopted different approaches to identify oligometastatic patients, a SBRT guided by functional imaging allows to postpone the beginning of systemic therapy, therefore the toxicity due to ADT, by almost 2 years.

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BOWEL LOOPS NEAR PROSTATE TARGET IN PROSTATE CANCER RADIOTHERAPY: A COMPLEX CASE SOLVED WITH THE USE OF A BELLYBOARD DEVICE

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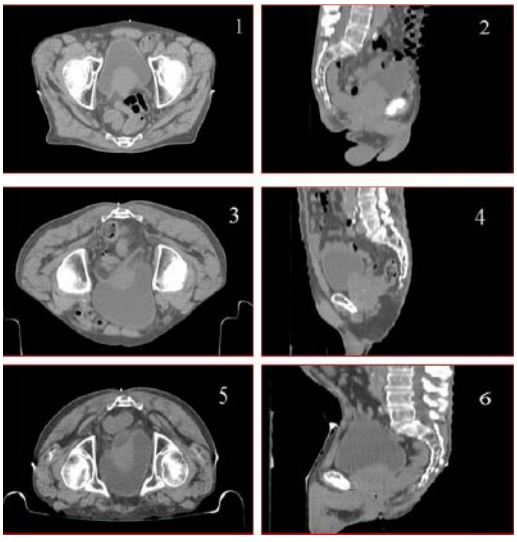
Aims: Pelvic radiotherapy is associated with the risk of acute small bowel toxicities such as pain, nausea and diarrhoea, and late toxicities such as bowel obstruction, fistulae and bleeding. It is traditionally delivered in a supine position for optimal stability. A prone position with a bellyboard device that, thanks to pelvic compression, allows for a dislocation of the loops of the patient's small intestine from the pelvic cavity can be used to reduce gastrointestinal toxicity. We describe a case of a patient

with prostate cancer who could not have undergone radical radiotherapy due to the presence of intestinal loops very close to the prostate, which contraindicated high radiotherapy doses.

Method: In November 2021 a 75-year-old patient with a clinical stage cT2c N0 M0 GS4+3=7 prostatic adenocarcinoma with an initial PSA of 10.8ng/ml, a prostatic volume of 90ml, and a neoadjuvant antiandrogen therapy just started, came to our department to undergo radiotherapy. Two months later he suffered a myocardial infarction, so that hormone therapy was stopped. Once his general condition improved, in March 2022 he underwent planning pelvic CT for radiotherapy, that showed bowel loops very close to the prostate (Figures 1-2). Their tolerance doses did not allow radical dose treatment of prostate cancer despite the use of advanced volumetric arc intensity modulated radiotherapy. A prone position with a bellyboard device (Contoura™ Bellyboard, CIVCO, 1401 8th St SE, Orange City, IA 51041, USA) was planned to dislocate bowel loops.



Figures 1-2-3-4.

Results: A first attempt to dislocate the intestinal loops failed due to incorrect positioning of the device (Figures 3-4); the second attempt was successful (Figures 5-6). The patient underwent radiotherapy on the prostate and seminal vesicles for radical intent up to 70 Gy (2,5 Gy/fraction, 5 fractions for week) to the prostate, and daily pre-treatment cone beam computed thomograpy positioning verify, with no urinary or intestinal side effects.

Conclusions: Prone positioning with a belly device is usually used in pelvic radiotherapy to reduce the dose of the small bowel thanks to their dislocation, but it could also be useful in the treatment of the prostate alone when, for particular anatomical conditions, the advanced technique is not sufficient to reduce the dose to the bowel within tolerable limits without reducing the dose to the target. Staff training in the use of the bellyboard is essential for the effective use of the device.

P244

DEFINITIVE RADIO-CHEMOTHERAPY AND INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) IN INVASIVE VAGINAL CARCINOMA: A MONOCENTRIC EXPERIENCE

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Aims: Vaginal carcinoma (VC) is a rare malignancy accounting for 1% to 2% of all gynecological cancers. Although surgery yields good local control (LC) and overall survival (OS) in selected cases of vaginal intraepithelial neoplasms and early (I–II) stages of VC, definitive radio-chemotherapy (RCT) followed by interventional radiotherapy (IRT, also called brachytherapy, BT) is considered an excellent option. The aim of this study was to report the results of our mono-institutional series of vaginal cancer patients treated with radio-chemotherapy followed by image- guided IRT.

Methods: We retrospectively analysed 16 patients with primary vaginal cancer who received RCT followed by IRT with curative intent between January 2019 and December 2021. The primary study end-point was the local control (LC), secondary end-points were the overall survival (OS), the cancer specific survival (CSS), disease free survival (DFS) and the rate and severity of acute and late toxicities.

Results: All patients received planned treatment. Twelve patients were stage II, 2 patients stage III and 2 stage IVB (International Federation of Gynecology and Obstetrics stages 2008). The median total dose of external beam RT was 45Gy (range 45Gy-60Gy). OncentraBrachy treatment planning system and a Flexitron (Elekta,

Stockholm, Sweden) device with a 192-Ir source were used for IRT treatment. The median IRT total dose was 28 Gy (range 10Gy-28Gy). All patients received cisplatin chemotherapy. The median duration of follow-up was 19 months (6-38 months). One-year LC, OS, CSS and DFS rates were 100%, 100%, 100%, 92.8%, respectively. In ten cases, acute toxicity was registered. There were four gastrointestinal G2, one genito-urinary G2, and five gastro/genitourinary G1, as well as three vaginal inflammatory G2. In ten cases, late toxicity was registered. There was one G3 stenosis, two G2 stenosis, and six G1 stenosis recorded. One patient was diagnosed with teleangectasia G1.

Conclusions: Definitive radio-chemotherapy followed by image-guided IRT is an effective treatment modality for primary vaginal cancer.

P245

EXCLUSIVE RADIOCHEMOTHERAPY *VERSUS* NEOADJUVANT RADIOCHEMOTHERAPY IN CERVICAL CANCER PATIENTS

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Aim: To compare outcomes in FIGO stage IIB-IVA cervical cancer patients treated with exclusive radiochemotherapy (EXC RTCT) versus to neoadjuvant radiochemotherapy (NAD RTCT).

Method: Between 2010 and 2020, 427 FIGO STAGE IIB-IVA cervical cancer patients were treated. We divided patients according to type of treatment: 116 (Group A) patients underwent to EXC RTCT (concurrent platinum-based chemotherapy plus a median of 45 Gy of external beam radiation and 28 Gy in 4 fractions of High Dose Rate brachytherapy); 311 (Group B) patients were submitted to NAD RTCT followed by radical surgery (concomitant platinum-based chemotherapy plus a median dose of 45 Gy of external beam on the whole pelvis).

Results: The baseline characteristics of the two groups are summarized in Table 1. There were no differences in the pattern of acute toxicity. With a median follow up of 40 months, the progression free and overall survival are the same in both groups, but it seems be a trend of significativity for a local control in favour of NAD RTCT. It could be caused from a different distribution of the stages, age and comorbidity between the groups.

Conclusions: NAD RTCT does not improve survival outcomes when compared with standard EXC RTCT even if there is a trend in terms of local control. Further prospective and randomized studies should be performed in order to solve the question about the standard approach in this setting of patients.

Table 1.

Characteristics	GROUP A EXCLUSIVE RTCT	GROUP B NAD RTCT	T-Student Test (p-value)
N° Patients	116	311	NR
Age (ys)	62	45	0.05
Histology			
• Squamous Carcinoma	103	273	
• Adenocarcinoma	12	34	0.92
• Others	1	4	
Grading			
1	3	10	0.14
2	36	166	
3	40	88	
NA	37	147	
FIGO STAGE			
IB2	0	4	
IIA	5	10	
IIB	25	170	
IIIA	1	8	0.005
IIIB	0	27	
IIIC1	54	71	
IIIC2	18	11	
IVA	10	7	
IVB	3	1	
Toxicity GI			
G0	68	177	0.11
G1	36	101	
G2	10	33	
G3	2	0	
G4	0	0	
Toxicity GU			
G0	89	236	00.94
G1	24	67	
G2	3	8	
G3	0	0	
G4	0		
Toxicity EMATO			
G0	85	187	0.30
G1	22	67	
G2	7	47	
G3	2	10	
G4	0	0	

P246

ATLAS-BASED AUTO-SEGMENTATION OF ORGANS AT RISK IN GYNAECOLOGICAL CANCER: INTRAUTERINE BRACHYTHERAPY VS EXTERNAL BEAM RADIOTHERAPY

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Aims: Accurate segmentation of organs at risk (OARs) and target volumes is crucial for radiation treatment planning but highly time-consuming. One commercially available solution is atlas-based auto-segmentation (ABAS, Elekta AB, Stockholm). It aims to reduce time consumption and inter- and intra-observer's variability, which may significantly affect dosimetric parameters. The purpose of this study was to compare ABAS performances in OAR contouring in external beam radiotherapy (EBRT) and intrauterine brachytherapy (IB).

Method: Ten different EBRT and IB patients, treated between 2019 and 2021, have been retrospectively selected to create two different atlases in ABAS. OAR contours (rectum and bladder) used to create the atlases were carefully defined by two skilled radiation oncologists. The library performances have been tested comparing manual and ABAS contours on other 13 EBRT and 16 IB planning CTs. The chosen metrics were the Hausdorff distance (HD) and the Dice similarity Index (DI). The EBRT and IB results were compared performing the Anova test to assess statistical significance (α=0.05).

Results: The auto-segmentation process requested about 6 minutes for each EBRT CT set and about 4 minutes for IB patients. The median HD values for EBRT and IB patients were 23.79 mm [14.81 – 42.56 mm] and 24.27 mm [13.04 – 35.20 mm] for the rectum, and 20.64 mm [12.00 – 34.95 mm] and 12.18 mm [6.00 – 27.06 mm] for the bladder, respectively. The median rectum DI values for EBRT and IB group were 0.64 [0.34 – 0.81] and 0.61 [0.30 – 0.79], respectively. On the other hand, the DI values for the bladder were 0.80 [0.36 – 0.87] and 0.89 [0.79 – 0.94]. The bladder results showed a statistically significant difference ($p << 0.05$), while the rectum results showed a non-statistically significant difference ($p > 0.05$) for both the studied metrics.

Conclusions: The longer auto-segmentation time in EBRT with respect to IB patients could be explained by the femoral- heads contouring and a longer CT scan. In these preliminary results, bladder segmentation showed higher accuracy for IB patients compared to EBRT patients: the use of a contrast agent in the bladder during the CT scan facilitated the correct organ interface delineation. Furthermore, rectum segmentation showed a slightly worse accuracy for IB patients, partially explained by anatomy modifications due to the applicator placement.

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INTEROBSERVER DELIENATION AGREEMENT IN CERVIX CARCINOMA INTERVERNTIONAL RADIOTHERAPY (BRACHITHERAPY)

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Aims: Interventional radiotherapy (IRT, also called brachytherapy), combined with external beam radiotherapy and chemotherapy, plays an essential role in the radical treatment of locally advanced cervical cancer (LACC). By using individual optimization of dwell-times and positions of 192Ir high-dose-rate stepping sources, it is possible a dose escalation to the target volume (high /HR/ and intermediate-risk /IR/ clinical target volume /CTV/), without exceeding the tolerance limits of organs at risk (OAR). With increasing conformity of dose delivery, the influence of interobserver contouring uncertainties on the ability to achieve uncomplicated cure becomes more critical. This study aimed to analyse the agreement between target volumes delineated by two observers on CT images for cervix cancer IRT according to accepted guidelines.

Methods: Ten consecutive patients with LACC, treated with curative intent, were included in this study. IR-CTV and HR-CTV were contoured on CT by two radiation oncologists respecting the recommendations of the Gynecological- Groupe Européen de Curiethérapie (GEC) and the European Society for Radiotherapy & Oncology (ESTRO) working group (VL: senior gynecological interventional radiation oncologist; BF: two-year experience in gynecological interventional radiotherapy). They were blinded to the staging images and their colleagues' contouring plans. The conformity index (CI) assesses the impact on interobserver variability. The CI, which agrees to contoured volumes, is derived from the relationship between the intersection of segmented volumes and their union ($V1 \cap V2 \cap Vn / V1 \cup V2 \cup Vn$). A high CI indicates low interobserver variability.

Results: The means HR-CTV for operators 1 and 2 were 19.50 cm^3 and 21.08 cm^3, respectively. The means

IR-CTV for operators 1 and 2 were 73.42 cm^3 and 67.53 cm^3, respectively. The mean CI for IR-CTV and HR-CTV was 0.77 and 0.71, respectively. Table 1 reports target volumes expressed in cubic centimetres, as contoured by the two radiation oncologists, as well as CI.

Conclusions: The CI index showed a good agreement between the two radiation oncologists, underlining the recommendations of the GYN-GEC-ESTRO working group that target contouring represents a successful help for the clinicians. The mentioned recommendations, such as the existence of specialized schools in interventional radiotherapy, may help to improve delineation reproducibility for image-guided adaptive radiotherapy; even to reduce doses to adjacent OARs

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ROLE OF RADIOTHERAPY IN PLATINUM-SENSITIVE OLIGOMETASTATIC RECURRENT OVARIAN CANCER: A VALID ALTERNATIVE TO DELAY SYSTEMIC TREATMENT

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Aim: Ovarian cancer (OC) represents the most lethal gynaecological malignancy, with approximately 80% of advanced OC patients experiencing a recurrence after primary treatment. The role of radiotherapy in recurrent OC has been recently explored. The aim of this study was to assess the efficacy of advanced radiotherapy at the time of the 1st platinum-sensitive oligometastatic recurrence.

Method: The present is a retrospective monocentric study. Patients with epithelial OC undergoing primary treatment from January 2010 to April 2019 were considered for study inclusion. Among those, patients treated with radiotherapy alone at the time of 1st platinum-sensitive oligometastatic recurrence were included. Patients underwent ablative radiotherapy on all oligorecurrent lesions (stereotactic body radiotherapy or intensity modulated radiotherapy). Patients with encephalic or vertebral recurrence were excluded. Response rate (based on RECIST 1.1 criteria), predictor of treatment response, and survival outcome were evaluated.

Results: In total, 31 patients met the inclusion criteria. Of them, 18 (58,1%) had a complete response, 7 (22,6%) a partial response, and 6 (19.3%) a progressive disease (Figure 1). Among them, 30 (96.8%) had a subsequent relapse, of which 22 (73.3%) were treated with chemotherapy while the remaining 8 (26.7%) underwent re-irradiation or thermoablation. The median interval between radiotherapy and the subsequent recurrence requiring chemotherapy was 16 months (range 4-126), with 18 (58.1%) patients having a subsequent recurrence requiring chemotherapy after 12 months or more. Upon univariate analysis, median platinum-free interval before radiotherapy in patients with complete/partial response was longer than in patients with progressive disease (23 vs. 11 months, p=0.06), although not statistically significant.

Conclusions: In our experience, ablative radiotherapy alone represents a valuable option in the treatment of 1st oligometastatic platinum-sensitive recurrent epithelial OC, providing a good response rate and allowing to extend the platinum-free interval. Further studies with longer follow-up are required to confirm our results and identify predictors of treatment response.

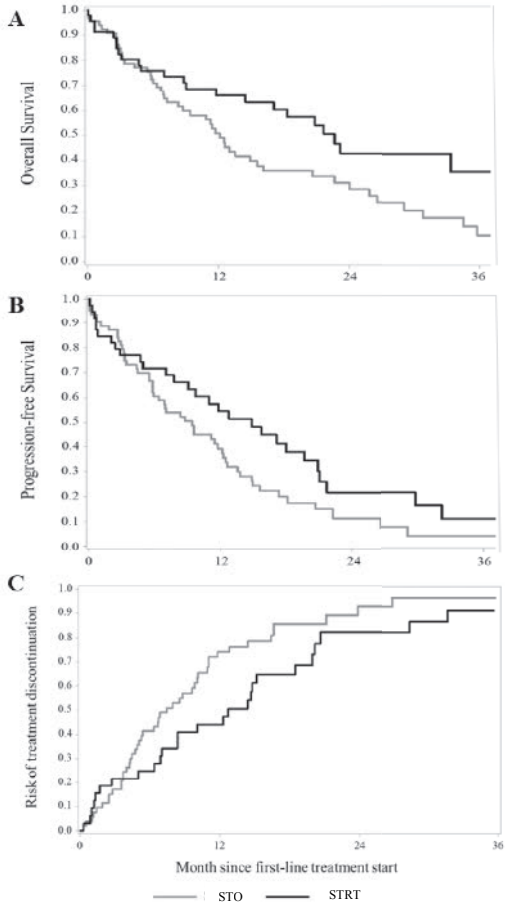

Figure 1. Kaplan-Meier estimates of overall survival (a), progression-free survival (b) and time-to-treatment failure (c) among patients with advanced NSCLC and synchronous brain metastasis treated with systemic therapy and advanced radiotherapy (STRT) or with systemic therapy only (STO). Footnote: in order to avoid immortal-time bias, in this analysis were only included patients who survived to the first three months of follow-up. For each patient, follow-up starts three months after the start of first-line systemic therapy.

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ADJUVANT INTERVENTIONAL INTRAVAGINAL RADIOTHERAPY (IRT-BRACHYTHERAPY) FOR STAGE I-II ENDOMETRIAL CANCER, WITH AN ALTERNATIVE DOSE SPLITTING SCHEDULE: A SINGLE CENTRE EXPERIENCE

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Aims: To test an alternative schedule of adjuvant intravaginal interventional radiotherapy (IRT-brachytherapy) with dose splitting every other day, following adjuvant pelvic external beam radiotherapy (EBRT) or not, in the management of stage I-II endometrial cancer.

Methods: Patients with stage I-II endometrial cancer, treated with surgery followed by high dose rate (HDR) - IRT vaginal adjuvant between 2016 and 2020 were included in this study. Among these, 36 patients (54.5%) underwent exclusive brachytherapy treatment, for a total dose of 21 Gy in 3 fractions every other day (7 Gy); the other 30 (45.4%) underwent brachytherapy treatment, for a total dose of 15 Gy in 3 fractions every other day (5 Gy), after adjuvant EBRT (45 Gy to 1.8 Gy per day were delivered). Gastrointestinal, genitourinary and vaginal late toxicity was assessed according to the CTCAE 5.0 scale during a mean follow-up period of 2 years.

Results: A total of 66 patients, median age 68 (range 35–91) years, were included in this analysis. The mean follow-up was 34.3 months in the exclusive adjuvant brachytherapy group, and 35.4 months in the adjuvant EBRT-IRT group. Acute gastrointestinal, acute genitourinary (arising within 3 months of brachytherapy) and vaginal late toxicities found in the exclusive IRT group were 0%, 30% (17% G1; 13% G2) and 2.8%, respectively. Acute gastrointestinal, acute genitourinary and vaginal late toxicities found in the EBRT-IRT group were respectively 53% (26% G1; 23% G2; 3.3% G3), 33% (30% G1; 3% G2) and 3.3%, respectively.

Conclusion: As expected, acute gastrointestinal and genitourinary toxicity appears to be worse in the group of patients undergoing adjuvant EBRT-IRT, while there appears to be no difference in late vaginal toxicity. The proposed brachytherapy treatment regimen, with subdivision of the dose every other day, seems to show a toxicity profile similar to that reported in the literature, especially in terms of delayed vaginal toxicity. Therefore, it is reasonable to propose it as a valid alternative to the already widely used weekly splitting regimens, with a reduction in the overall treatment period and an acceptable safety profile.

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INTENSITY-MODULATED RADIATION THERAPY OF VULVAR CANCER: IS IT REALLY SAFE?

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Objective: The role of intensity-modulated radiation therapy (IMRT) in the treatment of vulvar cancer (VC) is still debated. Given the rarity of this tumor, there is a lack of high level evidences on this topic in the current literature. The purpose of this systematic review is to analyze the current scientific evidences on the role of IMRT in VC, with particular attention on clinical outcomes, toxicity, and comparison between IMRT and 3D radiation therapy (3D-RT).

Methods: A systematic literature search was conducted on PubMed, Scopus, and Cochrane databases using the PRISMA methodology. Studies analyzing IMRT in VC patients were included. Primary endpoint was overall survival (OS). Local control (LC) and treatment-related toxicity were secondary endpoints. Whenever feasible, we analyzed any comparison between IMRT and 3D-RT in the treatment of VC.

Results: Six studies (200 patients) were included in this systematic review. Median follow up was 26.7 months (range: 19-34 months). Most patients underwent IMRT for VC, except for 15 patients, who underwent exclusive 3D-RT, and six patients who underwent both IMRT and 3DRT. Clinical outcomes (OS and LC) were reported heterogeneously, making it difficult to compare the different studies. In patients treated with preoperative IMRT the pathological complete response rates ranged from to 44% to 80.7%, with few out-of-field failures (<10%). Most patients experienced mild and acceptable toxicity. Only one fatal event was reported, probably due to the initial burden of the disease. One study comparing 3D-RT and IMRT reported a significant difference in acute grade 2-3 skin toxicity with 86.6% and 23.5% rates, respectively.

Conclusion: Given the lack of randomized clinical trial, the use of IMRT in the treatment of VC needs further clinical evidences. However, based on our analysis, the better conformation of the dose allows to reduce both incidence and severity of radiation-induced toxicity without affecting the tumor local control.

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ADJUVANT RADIOTHERAPY IN ENDOMETRIAL CARCINOMA WITH MICROCYSTIC, ELONGATED, AND FRAGMENTED (MELF) PATTERN: A SINGLE-CENTER EXPERIENCE

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Aims: Microcystic, elongated, fragmented (MELF) pattern of myometrial invasion has been proposed as a prognostic marker in patients with endometrial carcinoma (EC). Its prognostic and predictive effect still remains unclear. Aim of this study was to analyze the association of MELF pattern invasion with clinical pathology data and prognosis of the patients with MELF endometrial cancer treated by adjuvant external beam radiotherapy followed by brachytherapy boost.

Methods: Patients (pts) affected by endometrial cancer with microcystic, elongated, fragmented (MELF) pattern of myometrial invasion treated in our Institution between January 2017 and September 2021 were retrospectively enrolled in this study. All patients underwent total hysterectomy, bilateral adnexectomy and pelvic dissection followed by adjuvant radiotherapy. Adjuvant external beam radiotherapy was delivered to the pelvis with Volumetric Modulated Arc Therapy (VMAT) strategy for a total dose of 45 Gy, 1.8 Gy/fraction plus a brachytherapy boost on vaginal cuff for a total dose of 10Gy in 2 fraction weekly. When indicated, adjuvant platin-based chemotherapy was administered before the begin of radiotherapy.

Results: The clinico-pathological data of 39 pts (median age: 55 years; 2018 FIGO Stage IA: 5; IB: 10; II: 4; IIIA: 1; IIIC1: 19) were retrospectively analyze. Lymphovascular space invasion (LVSI) was described in 26 pts (66.6%), with focal LVSI in 5 pts and substantial LVSI in 21 pts. Median follow up was 24 months (range 8-64). Only one patient developed distant metastases 30 months after surgery. Median LC was 46 months; 2-ys and 4-ys LC and OS were of 95%. No correlation was found with type of surgery, number of removed and positive pelvic nodes and LVSI. The treatment was well tolerated with only one patient who developed a grade 2 gastrointestinal toxicity.

Conclusion: MELF appears to be one of the most aggressive patterns of myometrial invasion in endometrioid adenocarcinoma. The lack of international guidelines makes the management of this type of pattern controversial. In our experience, MELF endometrioid adenocarcinomas can be treated with adjuvant external beam radiotherapy, regardless of disease stage, with good results and acceptable toxicity.

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LONG TERM TOXICITY RATES AND QUALITY OF LIFE OF ADJUVANT EXTERNAL BEAM RADIATION THERAPY (EBRT) AND VAGINAL VAULT HIGH DOSE BRACHYTHERAPY (HDR-BT) IN ENDOMETRIAL CANCER PATIENTS: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: To evaluate the long-term toxicity rates and Quality of Life (QoL) of adjuvant External Beam Radiation Therapy (EBRT) followed by High Dose Rate Brachytherapy (HDR-BT) boost on vaginal vault, with or without chemotherapy (CT), in intermediate/high risk endometrial cancer patients.

Methods: From August 2018 to December 2021, we retrospectively analysed all patients with diagnosis of endometrial cancer and, subsequently, selected intermediate/high risks patients who underwent External Beam Irradiation, +/- chemotherapy, followed by HDR-Brachytherapy.

Results: In the period of observation, 54 patients with histological diagnosis of intermediate/high risk endometrial cancer were submitted to adjuvant Eternal Beam Radiation Therapy and High Dose Rate-Brachytherapy boost. All patients performed radical surgery and, among these, 44.4% of patients received lymphadenectomy. The EBRT-plan provided a total dose on Clinical Target Volume (CTV) of 45-50 Gy delivered in 25-28 Fx; 33,3% of patients received adjuvant platinum-based chemotherapy. The total dose of the HDR-BT boost was 12 Gy (44% of cases) and 15 Gy (56% of cases), both delivered in 3 consecutive fractions. The median follow-up was 24 months (range 6-46 months) and patients' long-term chronic toxicities have been evaluated according to CTCAE v4.0. In 15% of patients, G2 genitourinary toxicities such as recurrent cystitis and urinary incontinence have been detected, 11% of patients had G1 chronic diarrhoea and 5.5% of patients complained G1 recurrent pelvic pain. None of patients showed chronic toxicities ≥G3. A good Quality of Life (QoL) without chronic toxicities has been observed in the 68.5% of cases.

Conclusions: Our experience confirms that External Beam Radiation Therapy followed High Dose Rate-

Brachytherapy in intermediate/high risk endometrial cancer patients is feasible and well tolerated, with a low chronic toxicity profile and without detrimental impact on patients' Quality of Life.

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PREDICTIVE ROLE OF SARCOPENIA IN CERVICAL CANCER PATIENTS UNDERGOING CONCURRENT CHEMORADIATION. A SYSTEMATIC REVIEW OF THE LITERATURE

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Aims: The ability to predict response and outcomes in cervical cancer patients undergoing definitive chemoradiation would have the potential to allow for treatment adaptation and personalization. Several studies evaluated the condition of sarcopenia (SP), defined as the quantitative and functional impairment of skeletal muscles, for this purpose. The aim of this review is to summarize and analyze these reports.

Methods: A literature search was performed in PubMed, Scopus, and Cochrane library. After the removal of the duplicate papers, 82 reports were screened and of these 74 were excluded. Finally, 8 papers were included in this review and the following items were independently extracted by two authors: authors, publication year, treatment and patients' characteristics, method of SP evaluation, cut-off values, type of analysis, considered confounders, main results, and other findings.

Results: The results of the review are summarized in Table 1. The level of SP assessment for all analyzed studies was the third lumbar vertebra (L3) with most studies considering skeletal muscle index (SMI) as the reference (skeletal muscle area normalized for squared height) except for Kiytoki et al who considered only the reference area. Pre-treatment SP was found not significantly correlated with progression free survival (PFS) and overall survival (OS). However, Matsouka et al found a correlation between low pre-treatment SMI and psoas muscle index (PI) and parametrial involvement. Moreover, Han and colleagues found a significantly worse PFS only for patients with SP at baseline and who gained total fat during treatment. Post-treatment SP was associated with worse PFS if the SMI loss was at least more than: 5-10% or the iliopsoas muscle (IM) loss more than 15%. Three studies found a correlation between treatment-correlated SP and OS if the IM loss was more than 15% or SMI loss more than 7% or 10%, respectively. Two studies found that SMI loss was associated with higher risk of tumor recurrence if it was more than 5% and 10%, respectively.

Conclusions: The lack of correlation between SP pre-treatment with outcome prevents the use of this parameter to tailor the primary treatment. Conversely, the significant correlation between ΔSP and post-treatment SP could guide the choice of adjuvant therapies or the frequency of follow-up evaluations.

Table 1. Characteristics of the analyzed studies.

aHR: adjusted hazard ratio; ASMI: appendicular skeletal muscle index; BRT: brachytherapy; CCRT: concurrent chemoradiotherapy; CDDP: cisplatin; CT: computed tomography; CHT: chemotherapy; DRFS: Disease Relapse Free Survival; HR: hazard ratio; IM: iliopsoas muscle; IMAC: intramuscular adipose tissue content; LACC: locally advanced cervical cancer; L3-CT: CT scan at the level of the third lumbar vertebra; OS: overall survival; PFS: progression free survival; PMI: Psoas Muscle Index; RT: radiotherapy; SATI: subcutaneous adipose tissue index; SM: Skeletal Muscle, SMD: Skeletal Muscle Density; SMI: Skeletal Muscle Index; SP: sarcopenia; TATI: Total Adipose Tissue Index; VATI: visceral adipose tissue index; VFA: visceral fat area; VSMI: Volumetric skeletal muscle index °: normalized for squared-height

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THE ACCURACY AND TIMING OF MAGNETIC RESONANCE IMAGING (MRI) EVALUATION IN LOCALLY ADVANCED VAGINAL CANCER (LAVC) TREATED WITH CHEMORADIATION AND HIGH DOSE RATE BRACHYTHERAPY (HDRB) (CASE REPORT)

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Aims: Primary vaginal cancer (PVC) is a rare entity, 3% of all gynaecological cancers and occurs most frequently in elderly women. Squamous cell carcinoma is the most common histology. PVC is strongly associated with human papilloma virus (HPV). Given its rarity, treatment principles are extrapolated from established management data of cervical cancer. In cervical cancer the assessment of clinical response after chemoradiation is recommended 3-6 months after completion of treatment. Aim of this study was to evaluate the same features in LAVC.

Methods: We report the case of a 28-years-old patient with PVC T2N1M0 treated with definitive chemoradiation. Initial gynaecologic examination revealed a lesion of the middle third vagina, with complete obliteration of the left posterior fornix. Histology of this lesion confirmed a poorly differentiated squamous cell carcinoma of the vagina, p16+, Ki67 87%, HPV-. Diagnostic MRI showed a 45x1.7x49mm vaginal tumor extending to the vaginal fornices and to the left paracolpium with suspicious pelvic lymph nodes without significant lesions of the cervix or of the vulva. PETscan confirmed the vaginal tumor and a left iliac internal lymph node. The radiation with technique of volumetric modulated arc therapy (VMAT) and concomitant cisplatin was delivered. The vagina recieved a dose of 60 Gy/30 fractions (fr) of 2 Gy and cervix and regional lymph nodes recieved a dose of 50 Gy/25 fr of 2 Gy. At the end of chemoradiation MRI showed a 22x1.2x3mm vaginal residual tumor that was treated with intracavitary image guided HDRB using the tandem and ring applicator. The dose of HDRB delivered was 21 Gy in 3 fr of 7 Gy twice a week. We observed G0 genitourinary, G2 gastroenteric acute toxicity and G1 vaginal narrowing late toxicity according to Common Terminology Criteria for Adverse Events (CTCAE v.5.0).

Results: In our patient at 3 months after completion of treatment T2 weighted imaging MRI showed a residual disease of 12x3x8 mm and at 6 months revealed complete response (CR).

Conclusions: LAVC respond to definitive chemoradiation but the response takes time. Our results confirmed the accuracy of MRI for evaluation for CR and, furthermore, the optimal time to detect it was 6 months. We must use an adaptive way to modify the treatment as we observe the tumor response.

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ACTINIC APPENDICITIS FOLLOWING PELVIC RADIATION THERAPY: A CASE REPORT

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Aims: Pelvic irradiation for gastrointestinal or urogenital tumors is a very common treatment. We present a rare case of acute appendicitis following pelvic radiotherapy for cervix cancer.

Method: A 29-year-old patient diagnosed with stage IIIC poorly differentiated squamous carcinoma of the uterine cervix was referred in September 2021 to our Radiotherapy Department. Abdominal magnetic resonance (MRI) and 18FDG positron emission tomography (PET) showed bilateral involvement of the parameters and a right pelvic lymph nodal metastasis. She did not suffer from abdominal pain. The patient underwent pelvic radiotherapy with concomitant weekly cisplatin. Radiation therapy consisted of 25 daily fractions of volumetric modulated arc external beam radiotherapy, 5 fractions per week, up to 50 Gy on the pelvis, uterus, parametria and vagina (2 Gy per fraction), and 52.5 Gy on the pelvic lymph nodal metastasis (2.1 Gy per fraction). Treatment was well tolerated and completed in November 2021. Three days after the conclusion of radiotherapy, the patient underwent an abdominal MRI to evaluate tumor response before planned utero-vaginal brachytherapy. MRI detected appendicitis (Figure 1a), which was confirmed by an abdominal computed tomography (CT) (Figure 1b-c), showing an enlarged appendix with an enhancing wall, surrounded by extraluminal fluid. The patient underwent blood tests and clinical evaluation. Inflammatory markers (white blood cell count and C-reactive protein) were unremarkable; she had no abdominal pain; body temperature and physical examination were normal. The patient underwent antibiotic prophylaxis and was treated with utero-vaginal endocavitary pulsed-dose rate brachytherapy, 0.6 Gy/h, up to 32.4 Gy. The pelvic inflammatory situation was still evident and stationary on planning MRI (Figure 1d), but uterovaginal

brachytherapy was not deferred, and it was completed without complications.

Results: At last follow up, in May 2022, the patient was in good general conditions, still with no symptoms of appendicitis, and complete clinical remission of cervical cancer.

Conclusions: Asymptomatic actinic appendicitis is a rarely reported event after external beam radiotherapy. This is the second reported case. Its clinical significance is uncertain. In our case uterovaginal brachytherapy was performed without complications. Acute actinic appendicitis, if asymptomatic, seems to require no surgical intervention and no postponement of scheduled brachytherapy.

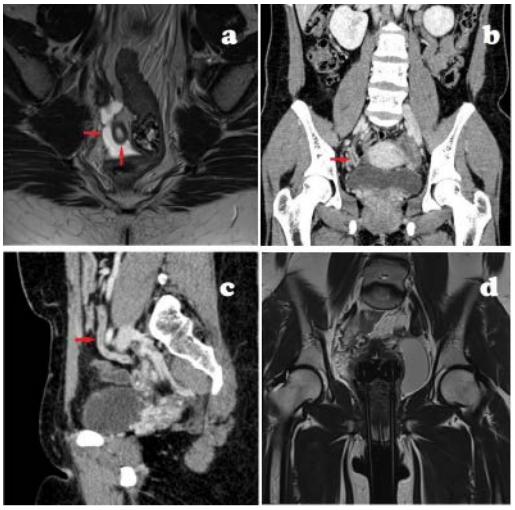

Figure 1. a: T2 weighted coronal RM image shows enhancing tubular structure with thickened and enhancing wall (up red arrow), surrounded by extraluminal fluid (right red arrow); b: contrast-enhanced CT coronal reconstruction shows in the right pelvis enlarged pelvic appendix and enhancing wall (right red arrow); c: contrast-enhanced CT sagittal reconstruction shows in the right pelvis enlarged pelvic appendix and enhancing wall (right red arrow); d: T2 weighted coronal RM image showing brachytherapy utero-vaginal applicator and right pelvic effusion.

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A RARE CASE OF RECTO-VAGINAL SEPTUM PRIMARY SQUAMOUS CELL CANCER

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Aim: Carcinoma of recto-vaginal septum (RVS) is an extremely rare entity. Surgey and adjuvant chemoradiation therapy seem to be the most common treatment option. However, since primary surgical treatment leads to mutilation by removing a large portion of vagina and the anal sphincter, primary platinum-based chemoradiation therapy could be considered.

Methods: In this report, we describe a case of a patient with RVS primary squamous cell cancer treated with radiochemotherapy.

Results: A 60 year old woman was having rectal and vaginal disconfort for a month duration. The patient underwent pelvic ultrasound which revealed a solid mass between the rectum and vaginas. CT of the chest abdomen and pelvis revealed a 3.5 x 3 cm mass with loss of the interventing fat plane with the rectus/anus posteriorly and the cervix/vagina anteriorly. This mass was confirmed by pelvic MRI. No suspicious lymph nodes or distant metastases were seen. The patologic report described a low grade squamous cell intraepitelial carcinoma p16 positive. PET/TC scan revealed intense tracer upatake in the mass in the rectovaginal septum. The patient was treated with combinated radiochemotherapy. Radiotherapy was delivered using a VersaHD platform and 6MeV photons. With conventional fractionation (2 Gy daily) and VMAT tecnique was delivered 50 Gy to internal iliac, exsternal iliac, presacral, obturator and inguinal lymph nodes, 60 Gy to mesorectum, rectum and vagina, 66 Gy RSV mass. Before each fraction isocenter position was verified by CBCT. She received weekly dose of cisplatin for 6 weeks. The treatment was well tolerated, we registred GI e GU toxicities G1. After 2 and 6 months of therapy, MRI revealed no imaging evidence of residual neoplastic mass.

Conclusions: In these case report radiochemotherapy resulted in a complete regression of RVS cancer. In June 2022, after 10 months of follow up the patient remains free of disease and asymptomatic.

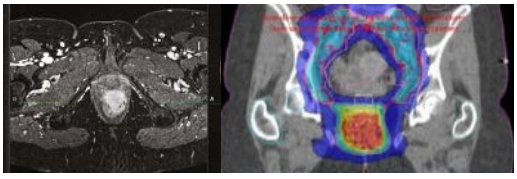

Figure 1.

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MELF PATTERN INVASION IN ENDOMETRIAL CARCINOMA EARLY STAGE, LOW GRADE: ADJUVANT STRATEGIES. EXPERIENCE OF THE UNIVERSITY HOSPITAL SAN GERARDO IN MONZA

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Aim: Early stage FIGO grade 1 endometrial carcinoma (EC) generally represent good prognosis disease; however, the detection of Microcystic, elongated, and fragmented (MELF) pattern is considered critical in this

group, because MELF is highly associated with lymph node metastasis and lymph vascular space invasion (LVSI). Whether the patients with low grade carcinoma require further therapy is still under investigation. In this paper we investigate the presence of MELF pattern in EC low grade and early stage as a contribution to the discussion on tumor board and decision for adjuvant therapy in our Institution

Method: We retrospectively reviewed all the patients with endometrial cancer who underwent hysterectomy at our institution between January 2021 to May 2022 and we considered eligible for inclusion patients MELF positive, early stage, and low grade. Among 26 patients 5 were included. Median age was 61.4 years. For two patients in stage IA, MELF was associated to LVSI and Isolated Tumor Cells (ITC) in sentinel node (SN). Three patients were in stage IB; only one MELF positive without other risk factors, and for 2 of them, MELF was associated to ITC in SN. No patient had mutations of mismatch repair proteins.

Results: Although there is limited evidence on the prognostic role of MELF, this pattern invasion was considered to be associated with poor prognostic factors such as LVSI and ITC. Patients who exhibited these features discussed at multidisciplinary team meetings ,experienced changes in the therapeutic management and were more likely to receive a treatment intensification either in the form of adjuvant radiotherapy if only LVS positive, or chemotherapy and /or radiotherapy if ITC positive, regardless the clinical stage and/or the grade. From our results it clearly emerges that nowadays there is no a consensus in adjuvant therapy for this group. It is still debated if adjuvant therapy with the integration of molecular features thought to be associated with worse outcomes, should change the clinical practice .

Conclusions: Most FIGO grade 1 in early stage have an excellent prognosis, however a minority will demonstrate a more aggressive clinical course. An early identification of such cases could offer additional treatment to women who may benefit. Only increasing the number of patients MELF positive by a multinstitutional survey it will be possible to reach a consensus on the opportunity of an adjuvant treatment in this particular group of patients.

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QUALITY OF LIFE AND SEXUAL FUNCTIONING AMONG ENDOMETRIAL CANCER PATIENTS TREATED WITH ONE –WEEK ADJUVANT HIGH-DOSE-RATE VAGINAL BRACHYTHERAPY SCHEDULE

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Aims: To examine quality of life (QoL) and sexual functioning in a series of patients with intermediate and high-intermediate risk endometrial cancer treated with exclusive adjuvant one-week high-dose-rate (HDR) vaginal brachytherapy (VBT) schedule.

Methods: Between July 2008 and October 2013, 55 patients with diagnosis of endometrial cancer were treated with adjuvant exclusive VBT. All patients had undergone surgical treatment with a laparotomy approach before VBT. Postoperative VBT was administered 6-8 weeks after surgery. Treatment was delivered to the vaginal vault using a Nucletron HDR unit with iridium-192 source at a dose of 21 Gy/3fractions of 7Gy each, three times a week, every other day, prescribed at 0.5 cm depth of vaginal wall and for 3 cm of the length from the apex. The QOL was assessed by the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30) and by EORTC cancer-specific Quality of Life Questionnaire (QLQ-CX24).

Table 1.

RESPONSE	INTERCEPT	COVARIATES			
		TIME	BMI > 30	AGE > 70	TIME*(BMI > 30)	TIME*(AGE>70)
Physical Functioning	97.739*	-0.022			0.042	-0.079*
Role Functioning	98.913*	-0.036*			0.047*	-0.045*
Fatigue	3.132	0.064*			-0.068*	
Costipation	4.523	0.022				0.057*
Diarrhoea	4.781*	0.053*				
Emotional Functioning	92.674*				0.085	
Social Functioning	98.796*					-0.065*
GES	13.461*	-0.048				0.175*
Symptom Experience	3.710*					
Body Image	96.688*					
Sex Worry	9.025*				-0.273	
Sex Activity	87.208*			13.395	-0.303*	0.102
Vaginal Function	89.002*					
Sex Enjoyment	57.964*	-0.004			-0.302	0.145

*Only significant estimates have been displayed. All values are significant at p=0.05. Estimates with a p-value < 0.01 have been indicated using a *, GES: Global Health Status, BMI: body mass index.*

Results: The median follow-up time was 92 months (range 42-162 months). The questionnaires were carried out respectively at 1, 3, 6, 12, 24, 36, 48 and 60 months

after the end of BT. Response rate to the questionnaire was 100% (n = 55). Nineteen patients (35%) answered all the questions of surveys, while 36 patients (65%) completed the surveys except for questions on sex activity, vaginal function and sex enjoyment. Longitudinal analysis during the 5-year follow-up period showed a statistically significant trend towards worsening of fatigue, constipation, and diarrhea. Overall physical functioning and role functioning was not impaired after VBT. Over the time sex enjoyment improve except for old patients. For emotional functioning, sex worry and social functioning there is no significant time-related effect.

Conclusion: One-week brachytherapy schedule to the vaginal cuff is generally well tolerated. QoL is not worsened by vaginal brachytherapy.

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WEEKLY HYPOFRACTIONATED RADIATION THERAPY FOR BASAL AND SQUAMOUS CELL SKIN CANCER FOR ELDERLY PATIENTS (≥ 80 YEARS): OUR EXPERIENCE

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Aims: Non melanoma skin cancer comprises basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), frequently occurs in people over 60 years (yrs). Generally, surgery remains the first choice intervention for definitive treatment, however, different factors can preclude the radicality of intervention, including patient's comorbidities, location of the tumor and the subsequent presence of a large uncorrectable surgical defect. Radiotherapy (RT) is typically an alternative choice for localized tumors and the standard regimen consist of a daily session (5 days per week) for 4-6 weeks. Hypofractionation schemes can increase the adherence of elderly patients (pts) to RT. We decided to treat elderly pts (≥ 80 yrs) with weekly hyprofractionated RT regimen.

Methods: 10 elderly pts were identified and treated with definitive electron beam radiation with total dose of 60 Gy delivered in 10 weekly fractions. We evaluated the efficacy in terms of clinical response. We take photos before RT and every weeks during RT, 1 month and 6 months after treatment's end. Clinical evaluation was performed weekly during RT, 1 month and 6 months after the end of RT, and response rate was assessed clinically by two radiation oncologists. Acute toxicity were grades according to RTOG criteria.

Results: Four pts with localized BCC and six pts with localized SCC were treated at our institution, with median age of 88.5 (range: 80-99 yrs). 6 pts (60%) were male and 4 (40%) were female. 5 (50%) had an ECOG Performance Status (PS) of 1-2 and 5 (50%) had a PS of 3. Patient characteristics are reported in Table 1. Site of lesions were: face (8 pts) and preauricolar region (2 pts). 9 pts (90%) completed the planned treatment, only 1 (10%) patient died before the end of RT. At the end of RT treatment, 30% of pts had a complete response and 60% presented partial tumor control rate. 1 patient died from other causes, presenting a partial response at the last radiotherapy session (DTF 42 Gy). After 1 month 6 pts (50%) had a complete response; after 6 months, 7 pts (70%) had a complete control rate. Eight (80%) had no toxicity, 2 pts developed acute toxicity, 1 of these had grade 1 toxicity and 1 grade 3.

Discussion: Elderly pts may not be fit to perform daily therapy in hospital, therefore they may benefit from a reduction in the number of fractions. Weekly hypofractionated RT is an effective option of treatment, with low acute toxicity and acceptable tumor control.

Table 1. Patients characteristic.

Characteristic	Value (%)
Gender	
Male	6(60%)
Female	4(40%)
Age (mean)	88.5
ECOG Performance Status	
1	3(30%)
2	2(20%)
3	5 (50%)
Life expentancy	
>10 aa	0%
<10 aa	100%
Comorbidities	
0-1	2 (29%)
2	5(50%)
>3	3 (30%)
Charlson Age-Comorbidity Index	
8-9	8 (80%)
7-6	1 (10%)
5-4	1 (10%)
Mobilization	
Si	4(40%)
no	6 (60%)
Histology	
BCC	4(40%)
SCC	6 (60%)

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HYPOTHYROIDISM AND THYROID NODULES IN PEDIATRIC HODGKIN LYMPHOMA SURVIVORS (HL-S) AFTER RADIATION THERAPY (RT)

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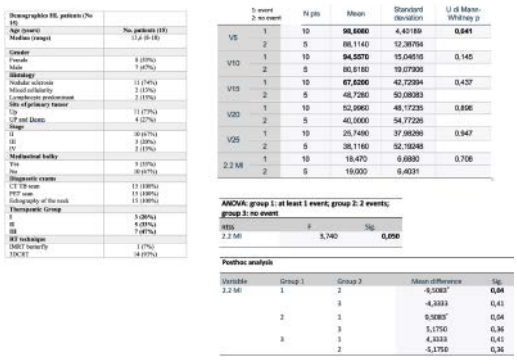
Aims: To evaluate the onset of hypothyroidism (HT) and thyroid nodules (TNs) after chemoradiation (CT-RT) for HL in pediatric patients (pts) with localization of latero-cervical and mediastinal disease.

Methods: Sixteen consecutive pts affected by classic HL were treated from 2009 to 2017 according to AIEOP LH-2004 protocol. 15pts (mean age 14yrs, range 8-18, Figure 1) were analyzed. Thyroid gland (TG) was contou-

red on RT simulation CT as two connected lobes below the thyroid cartilage. The thyroid volume (TV) found on simulation CT was confirmed by a thyroid ultrasound (T-US). During follow-up, HT was defined as elevated TSH or decreased fT4 levels (or both), and the presence of TNs was evaluated with a T-US. The VT receiving 5(V5),10(V10),15(V15), 20(V20), 25(V25) Gy, and the dose received by 2.2ml of TG were analyzed.

Results: Pts were divided into 3 therapeutic groups (GR): GR1 (3pts) received 3ABVD+RT because in partial response (PR) after CT; GR2 (5pts) received 4COPP/ABV+RT (3pts 14,4Gy because complete response (CR), two pts 2cycles of IEP +25,2Gy because PR); GR3 (7pts) received 4COPP/ABV, among these, 6 received 2 further COPP/ABV+RT because initial CR (3pts 25.2Gy and the other three 14.4Gy).One GR3 pt received 2cycles of IEP for PR + 25,2Gy and 3.60Gy boost on the sternum. PTV coverage was V90% 97, V95% 90, V107% 1,14 %; Mean VT was 7cc; Mean V5, V10, V15, V20, V25 was respectively 95, 92, 61, 49, 30 %; for 7pts (47%) 2,2 ml of their TG received more than 25Gy, for another mean dose to 2,2 ml was 15Gy. FU time was 8.5yrs; during FU 10pts (67%) showed TG alteration (between 3 and 8yrs after RT): 8pts (53%) developed one or more TNs (6 of them received 25,2Gy RT), 2pts develop only HT, 4pts both HT and TNs. One pt, (25,2Gy RT on right supraclavicular fossa) developed papillary TG cancer (pT2N1b) on left thyroid lobe (required surgery and I-131 radiometabolic therapy). The mean doses of V5,V10,V15 received by the TG were greater in pts who developed at least one TG alteration compared to those who did not have alterations, with V5 being statistically significant ($p<0.041$). When the sample was stratified in 3groups (one alteration,two alterations or none), the dose received by 2.2ml of TG was significantly higher in those with two alterations compared to those with one of the two alterations ($p<0.050$) Figure 1.

Conclusions: Treatment-related HT and TNs are frequent in pediatric HL-S:surveillance is mandatory to avoid late effects and allow for an early diagnosis of SNM.



	1: event 2: no event	N pts	Mean	Standard deviation	U di Mann-Whitney p
V5	1	10	98,6080	4,40189	0,041
	2	5	88,1140	12,38764	
V10	1	10	94,5570	15,04516	0,145
	2	5	80,8160	19,07306	
V15	1	10	67,5200	42,72394	0,437
	2	5	48,7260	50,08383	
V20	1	10	52,9060	48,17235	0,806
	2	5	40,0000	54,77226	
V25	1	10	25,7490	37,98288	0,947
	2	5	38,1160	52,19248	
2.2 MI	1	10	18,470	6,6890	0,708
	2	5	19,000	6,4031	

ANOVA: group 1: at least 1 event; group 2: 2 events; group 3: no event

	F	Sig.
2.2 MI	3,740	0,050

Posthoc analysis

Variable	Group 1	Group 2	Mean difference	Sig.
2.2 MI	1	2	-6,5083*	0,04
		3	-4,3333	0,41
	2	1	6,5083*	0,04
		3	2,1750	0,36
	3	1	4,3333	0,41
		2	-2,1750	0,36

Figure 1.

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VOLUMETRIC MODULATED ARC THERAPY TOTAL BODY IRRADIATION (TBI) AS A CONDITIONING REGIMEN TO HEMATOPOIETIC STEM CELL TRANSPLANT: A SINGLE CENTER EXPERIENCE

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Aims: Total body irradiation (TBI) can be part of the conditioning regimen for patients with leukemia undergoing hematopoietic stem cell transplantation. Aim of this study is to describe the experience gained at our institute with a dedicated EPID-based couch coupled for delivering a volumetric modulated arc therapy (VMAT)-based TBI.

Method: Selected patients underwent a total body CT in prone and supine position two weeks before treatment. A vacuum positioning cushion was used for immobilization. An experienced radiation oncologist was responsible for delineating the treatment target (whole body) and organs at risk. To limit the mean lung dose below 10 Gy, customized lung shields were produced for each patient using a 3D printer. Subsequently, a highly customized plan was calculated using Pinnacle TPS (Philips Radiation Oncology Systems, Fitchburg, WI). A dedicated couch with integrated EPID panels for performing online setup imaging and accurately positioning the printed lung blocks was used before delivering TBI, in supine and prone position. The prescribed dose was 12 Gy in twice daily fractionation (2 Gy per fraction), delivered by single modulated sweeping-arc technique.

Results: A total of 16 patients (median age: 33 years, range: 8 – 56) were treated at our Institute from April 2021 to April 2022. Conditioning chemotherapy before TBI was given to 11 out of 16 patients, in the remaining cases it was performed after radiation therapy. The dedicate couch with integrated EPID panel allowed a reproducible patients and lung shields positioning in all cases. The treatment was completed correctly by the totality of the proposed patients, and it was well tolerated overall. During three days of TBI treatment 2/16 patients developed parotitis G1, 6/16 patients developed nausea G1, 5/16 patients developed asthenia G1, G1 diarrhoea was described in a single case. All patients had leukopenia G2-3, mainly due to the previous chemotherapy conditioning regimen. Hematopoietic stem cell transplantation was performed successfully for all patients. With a median follow-up of 7 months (range: 2 – 14), no cases of disease

relapse have been reported.

Conclusions: The dedicated EPID-based couch VMAT TBI and the 3D-printed blocks proved to be a valid and feasible technique with well-manageable side effects that allowed us to achieve excellent reproducibility while keeping patient discomfort to a minimum. A prolonged follow-up will be needed for evaluation of late toxicities.

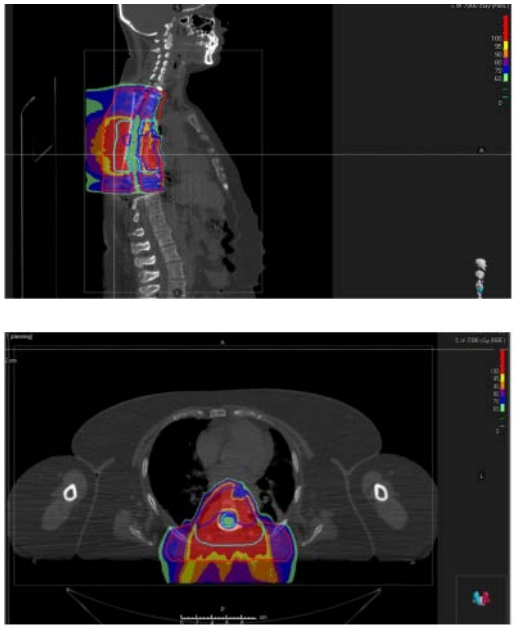

Figure 1. Axial and sagittal slice and dose distribution of a patient with thoracic chordoma blue line: PTV 74 Gy (RBE), sky blue line: PTV 70 Gy (RBE): red line: PTV 54 Gy (RBE).

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ELECTRONIC BRACHYTERAPY FOR THE TREATMENT OF CUTANEOUS LYMPHOMA: SINGLE CENTER EXPERIENCE

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Aims: Primary cutaneous lymphomas are a rare and heterogeneous group of malignancies often remaining localized. Radiotherapy is one of the most effective treatment modalities for both T-cell and B-cell lymphomas in the curative and salvage setting. Different radiotherapy modalities can be used electrons as well as low energy X rays. The purpose of this analysis is reporting outcomes of cutaneous lymphomas patients (pts) treated with local electronic brachytherapy (eBRT) to the involved site.

Methods: Data was extracted from case records for pts who had been treated with eBRT between October 2016 and January 2022. Data on histological type, staging, radiotherapy doses used, sites treated, systemic treatment, and outcomes of treatment were obtained and analyzed.

Results: Six male pts and 8 female pts with the median age of 67 (range 26-76) were treated by e-BRT for this condition with a total of 43 lesions. T-cell lymphomas constituted 39.5% of the diagnoses and 60.5% were B cell lymphomas (MZL 11.6%, FCL 18.6%, recurrence of DLBL 23.3%). Pts presenting stage I single lesion were 30.1% and 46,6% were treated for multi-site recurrences. Thirty-six lesions (83.7%) received 40 Gy, 9.3% 30 Gy and 7% 36 Gy. All treatments used conventional fractionation. Acute G1 and G2 RTOG score toxicity were showed in 39.5% and 60.5% respectively of the treated sites. Late G2 toxicity was scored 18.2% of the sites while 6% presented late G1 toxicity. No acute nor late toxicity > G3 has been recorded. Median follow up was 6 months (range 3-66). All pts obtained a complete response and are alive with free from in field recurrence. Recurrence in a different site was experienced in 20.9% of cases. Median time to progression was 7 months. Rituximab has been used after progression in most cases.

Conclusions: Radiotherapy is an important part of the treatment of cutaneous lymphomas, either as the sole treatment or as part of a multimodality approach. Electronic BRT is a feasible and effective treatment modality with excellent local control and good cosmetic results.

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TOTAL BODY IRRADIATION (TBI) AND HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT) AFTER CAR-T CELLS FAILURE: AN UNUSUAL CASE OF LYMPHOMA

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Aim: To describe an unusual case of transformed and multi-treated lymphoma in a patient (pt) undergoing TBI and subsequent HCT.

Methods: In November 2019, a 37-year-old male was diagnosed with a grade 2 Follicular Lymphoma (FL), stage IIIB high risk, with bulky disease. The pt was refractory to first line therapy with Obinutuzumab - CHOP (Cyclophosphamide, Doxorubicin, Vincristine and Prednisone); secondly to Rituximab-DHAP (Cisplatin, high-dose Cytarabine and Prednisone) and a bispecific antiCD20-antiCD3 antibody was performed after the diagnosis of DLBCL (Diffuse large B-cell Lymphoma), germinal center B-cell (GCB) like, transformed from FL. A new lymph node biopsy revealed a diagnosis of DLBCL,

GCB-like, with the expression of pan-B-cell antigens, including CD19 and CD20. The fluorodeoxyglucose (FDG) positron emission tomography (PET) showed a progression disease (PD). After lymphocyte-apheresis and bridging therapy the pt underwent a single infusion with CAR-T. The PET scan at day +30 showed a PD, the patient underwent a biopsy of abdominal lymph nodes. The diagnosis was of Hodgkin-like B cell lymphoma, with a defective B-phenotype due to the lack of CD20 and CD19 expression. The pt was started at 3 cycles of Pembrolizumab with further PD and subsequently was ultimately treated by Brentuximab-vedotin with complete remission (CR) after 6 cycle. In the light of the CR, HSCT previous TBI was proposed.

Results: the pt was treated with TBI high dose, twice daily 2-Gy fractions given over 3 days (total dose 12 Gy) with VMAT technique. Two computed tomography image sets were performed, with a slice thickness of 4 mm. The target volume is whole body, including the skin. Were contoured: heart, lung right and left, diaphragm right and left, hilum lung right and left. The contouring of such structures is necessary for the definition of lung shielding lead blocks. The TBI treatment plans were generated using the RapidArc™ software, provided within the Eclipse™ treatment planning system. The TBI was performed with a dedicated bed and the addition of a spoiler. In our case the lungs were the only OAR (mean lung dose accepted 8-10 Gy). The pt well tolerated TBI and at + 6 days underwent HCT. At day +30 after HCT showed cutaneous and ocular graft versus host disease.

Conclusion: At months +6 after TBI the pt reported CR. In our case the TBI and HCT has been a valid therapeutic option for a pt with pluri-treated lymphoma.

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SAFETY AND EFFICACY OF RADIOTHERAPY IN PRIMARY CARDIAC SARCOMAS: A SINGLE INSTITUTION EXPERIENCE

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Aim: Cardiac Sarcomas (CS) are extremely rare diseases with poor prognosis. No standard therapies have been established so far. Surgery (S) is the cornerstone of treatment and few data are available on the role of Radiotherapy (RT). The use of RT on the heart is challenging due to toxicity to cardiac structures. New RT techniques such as IMRT, VMAT, TOMO and SBRT allow to deliver a higher dose of radiation to the tumor while sparing surrounding structures. Few data about the safety and efficacy of cardiac RT for CS are available.

Methods: We retrospectively analyzed a series of patients (pts) with CS treated at our Institute with combined modality treatment (CMT) including RT, in terms of safety (according to CTCAE v5.0) and efficacy.

Results: Between 1999 and 2019, we identified 31 consecutive pts (13 females and 18 males) with median age 49 yrs (22-72 yrs) and diagnosis of primary CS, treated with CMT. The most frequent histologies were angiosarcoma (29%), leiomyosarcoma (19%), UPS (16%) and MPNST (10%). Tumor sites were right atrium (39%), left atrium (38%), left ventricle (6%), right ventricle (4%) and other sites such as pulmonary artery and vena cava (13%). Overall 21 pts (68%) underwent S on the primary tumor and 27 pts (87%) received chemotherapy, mostly with anthracycline based regimens. RT was used in 21 pts (68%), with adjuvant intent in 52%, definitive in 29%, neoadjuvant in 14% and palliative in 5% of cases. RT was administered with TOMO in 80% of pts at the dose range of 30.6-62.5Gy. 12 pts (57%) received 45Gy/25fr to PTV1 and SIB of 54Gy to PTV2 (GTV plus margins). The RT plan was prepared using a 4D-CT scan integrated with Ecocardio (EC), Cardio-CT and Cardiac MRI to define GTV, jointly with the cardiologist. CTV encompassed the GTV with a 15mm margin adjusted for anatomical structures. PTV was created by adding 5-mm expansion to CTV. Weekly EC and ECG +/- Holter were performed. In pts who underwent RT, mOS and mPFS were 32.5 and 18.6 months, respectively. Acute toxicities were mostly G1-2 oesophagitis, dyspnea, thoracic pain, cough and hematological; we observed a case of G3 thrombocytopenia the only occurrence of late toxicity. Cardiac acute toxicities were: atrial fibrillation in 2 pts, pericarditis in 2 pts and atrial flutter in 1 pts.

Conclusions: CS are very rare diseases and a multidisciplinary approach is mandatory. RT integrated with chemotherapy and S appears safe and feasible. Despite the limitations of this study, encouraging survival data were observed with RT.

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CLINICAL OUTCOMES IN PATIENTS WITH CHORDOMAS AND CHONDROSARCOMAS OF THE SPINE TREATED WITH PENCIL BEAM PROTON THERAPY

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Purpose or Objective: Spine chordomas and chondrosarcomas are rare, locally aggressive and radio-resistant tumors located along the axial spine. Surgery is considered the treatment of choice, however local recurrence rate is high and adjuvant radiotherapy improves local control. Proton therapy has the potential to deliver high radiation doses, which may improve the therapeutic ratio when compared with conventional radiotherapy. The aim of our retrospective study is to evaluate the toxicity profile and clinical outcome of patients (pts) with spine chordomas and chondrosarcomas treated with definitive postoperative or re-irradiation pencil beam scanning proton therapy at Trento Proton Therapy.

Material and Method: Between October 2014 and December 2021, 125 pts with histologically proved diagnosis chordomas and chondrosarcomas of the spine were irradiated with proton therapy (PT) at our institution. The mean age of patient population was 63 years (range:18-86). Of the 125 spine chordoma and chondrosarcoma pts, 83 were male and 42 female. There were 101 Chordomas (80.8%) and 24 Chondrosarcomas (19.2%). Tumor lesions were located as follows: sacrum- coccyx n=38, lumbar n=32, thoracic n=29, cervical n=21, and 5 cranio-cervical junction. Median diameter at the time of treatment was 114 mm (range 13-146). Fifteen lesions were only biopsied and treated with exclusive PT. Forty-six and 63 lesions had been treated with one or ≥2 surgery respectively; 94 patients had gross residual disease at the beginning of PT; 76 cases were treated with adjuvant intent, 1 with neo-adjuvant intent, 16 cases were re-irradiation, 12 of them after photons (total dose range 30-64,8 Gy). A conventional fractionation technique was used for 109 treatments, in 4 cases a Simultaneous Integrated Boost and in 12 cases a mixed technique. All pts were treated with active beam scanning PT. Single field optimizations was used for 80 pts, multifield optimization for 36 and mixed for 9. All pts with a diagnostic biopsy or subtotal resection were evaluated by a surgeon before radiation therapy for further surgical consideration. PT was delivered with standard fractionation (1,8-2,0 Gy (RBE)/fraction and the vast majority of patients, received 3 clinical targets volume dose 66, 31 pts 2 and 28 pts one clinical target volume dose respectively. Mean prescribed total dose was 70 GyRBE (range 66-76 GyRBE) for HR PTV, 66 GyRBE (range 60-70 GyRBE) for IR and 54 GyRBE (range 50-60 GyRBE) for LR PTV. Seventy-seven pts had side effects due to surgery or disease at the time of PT.

Results: PT was well tolerated, 120 pts completed it without breaks related to acute side effects. Five pts interrupted definitively the treatment respectively due to: n=1 disruption of bone reconstruction system (re-irradiated case), n=1 distal disease progression and n=3 general conditions decline. Acute skin G3 toxicity was the most common adverse effect experienced in 17 pts. No other ≥ G3 acute side effects were reported. Late Grade 3 side effects included 1 skin discoloration, 1 dysphagia, 1 paresthesia, 1 rectal colitis, 1 skin infection,3 disruption of bone reconstruction system, 5 bone fractures and 14 pts experienced neuropathic pain NRS≥ 5. The median follow-up was 27 months (range 2-78). At the time of this analysis 67 (53,6%) pts present local control disease. Across all time points 40 (32%) pts experienced disease recurrence: 24 local recurrence (18 chordomas and 6 chondrosarcomas), 4 distant recurrence (3 chordomas and 1 chondrosarcomas),12 pts died for disease progression (10 chordomas and 2 chondrosarcomas). Salvage treatments after PT failure included surgery, systemic therapy and Best Supportive Care.

Conclusions: Our data confirm that pencil beam scanning proton therapy for chordomas and chondrosarcomas is both safe an effective considering the high doses delivered and the proximity of adjacent critical structures the toxicity late profile is acceptable. A longer follow-up is obviously needed to gain more robust data for late toxicity and long term disease control.

Figure 1.

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PREOPERATIVE CONCOMITANT GEMCITABINE AND EXTERNAL-BEAM RADIATION THERAPY FOR PATIENTS WITH EXTREMITY AND TRUNK SOFT TISSUE SARCOMA

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Aims: To evaluate safety, toxicity, wound complications and survivals in a consecutive cohort of patients with extremities and trunk soft tissue sarcomas (STS) addressed to neoadjuvant chemoradiotherapy with Gemcitabine after high-dose induction chemotherapy.

Methods: patients affected by STS of the extremity or trunk, treated at our institution, were retrospectively reviewed for the analysis. Patients were treated with neoadjuvant chemoradiotherapy with weekly Gemcitabine after induction chemotherapy.

Results: From November 2018 to May 2022, 20 patients (11 males and 9 female) with a median age of 65.5 years affected by STS were treated with radiotherapy and concurrent chemotherapy with neoadjuvant intent. Chemotherapy consisted of Gemcitabine 300 mg/mq administered weekly during radiotherapy after 3 cycles of HD ifosfamide i.c . The mean target size was 7.9 cm (4-20 cm). In all cases R0 resection was obtained with 8 Complete pathological response. In only four (14%) patients wound complications occurred. 85% of patient completed the induction treatment. All patients started concurrent chemoradiotherapy; Only one patient had grade 3 hematological toxicity with temporary interruption of treatment for 4 days. 2 year LC and 2 year PFS were 97.3% (median not reached) and 87.6% (median 29.4 months).

Conclusion: Preoperative radiotherapy with gemcitabine resulted well tolerated achieving high rates of clear margins resections and good rate of complete pathological response, without increase of toxicities and good compliance. This combination should be investigated on a larger number of patients in order to confirm its feasibility and efficacy.

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STEREOTACTIC BODY RADIATION THERAPY FOR THE TREATMENT OF PULMONARY METASTASES FROM SARCOMA. OUR EXPERIENCE

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Aims: This retrospective study presents the experience from our Hospital with the largest series of SBRT for patients (pts) with pulmonary metastases (PM) from bone and soft tissue sarcomas (STS).

Methods: 63 pts have been treated at our Hospital with SBRT for bone and STS pulmonary metastases from 2010 to 2018 to a total of 154 PM. Free breathing CT scan with slow rotation time was performed. Gross tumor volume (GTV) and the clinical target volume (CTV) were considered equivalent. The prescription dose and fractionation schemes were very variable based on the site, size and histology. The most commons were 55 Gy/5 (19%), 54 Gy/3 (12%) 60 Gy/8 (8%). Biologically effective dose (BED) was calculated assuming an $\alpha\beta = 10$ for tumors. The median BED prescribed was 105 Gy. The dose was prescribed to the 80% isodose. Set-up control was done through a daily cone-beam CT. After SBRT, pts were followed with chest CT every 3 months for the first year then every 6 months. Local control (LC) was defined as the absence of disease progression in the treated site. Acute and chronic toxicity was graded according to RTOG criteria.

Results: 63 pts were eligible with 154 PM treated. The median PM treated for pts was 2. The median age at diagnosis was 41 years. Of these pts 19 were female and 44 male. Twelve patients had PM at diagnosis, the others had developed metastatic at a median of 20 months. 40 patients (63%) underwent at least one pulmonary metastasectomy, 49 pts (78%) received chemotherapy before first SBRT treatment. The median number of PM treated in each course was one. The median FU from SBRT was 34 months. The LC rate at last available radiological follow-up was 92.2%. Analysis was conducted on 150 lesions. At the last follow-up 20 pts were alive with disease, 7 alive without disease, 36 dead due to disease progression. The 2-year OS from evidence of lung metastases was 93.7% and 5-year OS was 50.4%. The OS from first SBRT at 1-years was 81.%, at 2-years was 66.3% at 5-years was 39.9%. No severe, grade III–IV toxicity was observed.

Conclusion: SBRT for sarcoma pulmonary metasta-

ses produces a good local response; however, pts remain at risk of distant and within the lung failure. Although 5-year survival remains low, SBRT can have an important role in the treatment of this disease, particularly appealing for patients who are not fit for surgery or decline surgery. Multidisciplinary discussion and personalized medicine are important to determine the best option.

P268

LOCAL CONTROL AFTER METASTASES-DIRECTED THERAPY IN OLIGOMETASTATIC SOFT TISSUE SARCOMA PATIENTS

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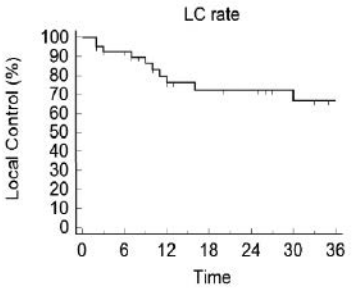
Aims: Soft tissue sarcomas (STS) are rare malignancies that represent approximately 1% of adult cancers. In STS patients experiencing advanced or recurrent disease, therapeutic options are limited due to poor responsiveness to standard chemotherapy (CT). Metastases-directed therapy (MDT), like metastasectomy or stereotactic radiotherapy (SBRT), can be considered in selected cases in order to improve disease control. Our aim was to assess local control (LC) and to identify predictors of treatment failure in oligometastatic patients after MDT.

Method: We retrospectively analyzed 19 consecutive patients treated for 42 metastases at our institution from 2013 to 2022 with either surgery or SBRT. Oligometastatic disease was defined as no more than 5 extra-cranial metastases. Clinical (primary site, synchronous onset, pulmonary vs extrapulmonary metastatic site) and treatment related data (type of MDT, use of adjuvant CT) were collected. Local control was defined as lack of radiological progression (according to RECIST criteria v1.1) of the treated site until last follow-up or death of the patient. Statistical analysis was performed to assess variables associated with LC, using MedCalc v20.111.

Results: Out of 42 metastases, 21 were treated by SBRT and 21 by surgery. Out of 19 patients, 14 (74%) underwent adjuvant CT. Primary tumors were located to the limbs in 13 patients (68%) and to the trunk in 6 patients (32%). Oligometastases onset was synchronous (within 6 months from primary diagnosis) in 5 cases (12%) and metachronous in 37 (88%). SBRT was performed in 3-5 fractions to a total dose of 30-60 Gy: median BED10 was 105 Gy (range 35.7 - 151.2 Gy). LC rate was 80% at 1 year and 72% at 2 years (Figure 1a), median not reached. At univariate analysis, none of the aforementioned variables were significantly correlated with LC. No >G2 toxicities were observed in all treatments.

Conclusions: In this cohort of oligometastatic STS patients, MDT achieved a satisfying and durable LC rate, with no statistically significant difference between those treated with SBRT or surgery (Figure1b) . Despite the supposed radioresistance of STS, SBRT proved a safe and effective treatment option in this setting.

a. Kaplan-Meyer plot for local control.



b: Kaplan-Meyer plot for local control in metastases treated by surgery versus SBRT.
No statistically significant difference was observed.

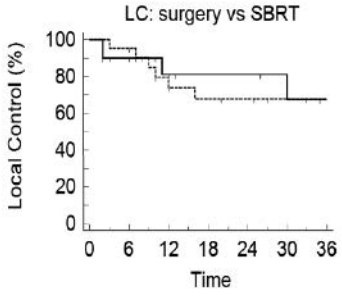


Figure 1.

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SACRAL INSUFFICIENCY FRACTURES AFTER CARBON-ION RADIOTHERAPY FOR SACRAL CHORDOMA: IMPACT OF DOSE DISTRIBUTION AND LET

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Aims: There is very little data on sacral insufficiency fracture (SIF) incidence following pelvic carbon-ion RT (CIRT). Our study aims to evaluate the occurrence and the pattern of SIFs in patients underwent curative CIRT for sacral chordomas and the correlation between SIFs

and relative biological effectiveness (RBE)-weighted dose (DRBE) and dose-averaged Linear Energy Transfer (LETd) distributions.

Methods: Between 2013 and 2021, 54 patients with histologically proven sacral chordoma were treated with CIRT. The total dose ranged from 70.4 to 73.6 Gy(RBE), in 16 fractions. The volume of fractures (VF) reported during follow-up were contoured on the corresponding MRI and graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. We analyzed dose-volume histogram (DVH) DRBE and LETd distributions of the sacral bone, looking for a correlation between VF and the volume of sacrum (VD) receiving a dose D (ranging from 20 to 75 Gy(RBE), in steps of 5 Gy(RBE). For the VF, the minimum, median and maximum DRBE and LETd and the volume percentage receiving a LETd > 50 keV/μm (V50keV/μm) were compared to the healthy bone average values.

Results: The median follow-up was 34 months (range, 2 – 86 months). SIF was observed in 27 patients (36%). Multiple or single fractures were found in 69% and 31% of patients respectively, the majority located in the sacral wings. SIF of grade 1 and grade 2 was scored in 23 (85%) and 4 (15%) patients, respectively. The VD of sacrum receiving doses D ≥ 55 Gy(RBE) were significantly higher in the fractured patient cohort. Analyzing LETd distributions in the fracture volume the average minimum LETd was significantly higher, while no difference was found in V50keV/μm.

Conclusions: The SIF occurrence recorded in our patient population is in agreement with previous study using particle therapy. The volume of sacral bone receiving high doses significantly increase the risk of developing SIF. The data of other 29 patients are currently being analyzed. Other clinical factors (*i.e.* age, sex, prior surgery, concomitant medication, body mass index) are currently under evaluation in order to develop a patient-specific risk stratification to minimize severe clinical complications and set-up (pre)-rehabilitative strategies.

P270

PROTONTHERAPY TREATMENT FOR SKULL BASE CHORDOMA AND CHONDROSARCOMA: RESULTS OF THE CENTER OF TRENTO

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Aims: Skull base chordomas (C) and chondrosarcomas (CS) are locally aggressive tumors located adjacent to critical structures. Radiotherapy is used both as an adjuvant treatment to surgery and as a radical one. The aim of our retrospective study is to report the experience of the Trento Proton Therapy Centre in terms of toxicity profile and clinical outcome

Material and Method: Between June 2015 and April 2022, 62 patients (Pts) with skull base C and CS were irradiated with proton therapy (PT). Mean age was 48.6 years (range: 3.7 -83.1). There were 53 C (85.5%), and 9 (14.5%) CS. Location was: clivus n= 59, petroclival region n=2 and anterior cranial fossa n=1. 49 pts were treated at first diagnosis, 13 after recurrence. Surgery was performed at least once in all but 2 patients; 54 cases had gross residual disease at the beginning of PT, 8 cases were without gross disease. Six cases were re-irradiations. Side effects were graded according to CTCAE5.0.

Results: All but two pts completed their treatment (one distant progression and one general conditions decline). Mean overall treatment time was 50.1 days (range: 36-58). All pts were treated with active beam scanning PT. Technique was conventional in 38, Simultaneous Integrated Boost in 2 and mixed in 22 pts. Single field optimizations was used for 44 pts, multifield optimization for 17 and mixed for 1. Mean high-risk (HR) PTV volume was 58.8 cc (range 2.2-335.8); mean low-risk (LR) PTV volume was 97.8 cc (range 19,4 - 266,9). Mean prescribed total dose was 70.0 GyRBE (range 54-74 GyRBE) for HR PTV and 54.0 GyRBE (range 50-59.5 GyRBE) for LR PTV. No acute or late ≥ Grade (G)4 side effects were reported. Acute G3 toxicity occurred 7 times; late G3 toxicities 15. Median follow-up was 31.3 (range: 0.9- 82.4) months. All 8 pts treated without gross disease are alive without any relapse. Of the 54 pts with gross disease: 39 are alive with local diseasecontrolled, 1 is alive with local and distant progression, 5 are alive with local progression, 4 died of local disease, 3 died of other causes, 2 died of local and distant progression. 13 local relapses occurred between 1.0 and 53.8 months (mean: 20.2), in 3 cases associated with distant ones, 1 successfully managed with further radiotherapy

Conclusions: PT allows to deliver high dose of radiation therapy in a very critical setting. Early results are encouraging but a longer follow-up is needed to gain more robust data for late toxicity and long term disease control.

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MULTIDISCIPLINARY APPROACH OF ADVANCED-STAGE ALVEOLAR RHABDOMYOSARCOMA OF THE MAXILLARY SINUS IN ADULTS: A CASE REPORT

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Aims: Alveolar rhabdomyosarcoma (ARMS) is a rare soft-tissue malignancy that is common in children, but it

is extremely rare in adults. Since the clinical course and the treatment strategy for advanced disease are not well established yet, we emphasize the role of multidisciplinary (MD) approach in this setting of patients.

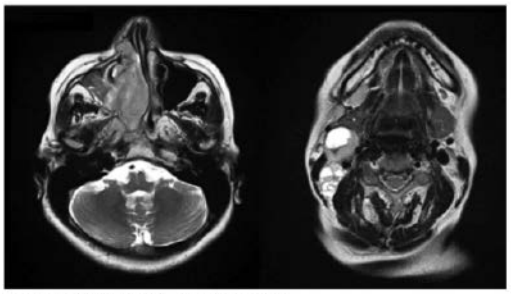

Figure 1. Pretreatment MRI images of the mass.

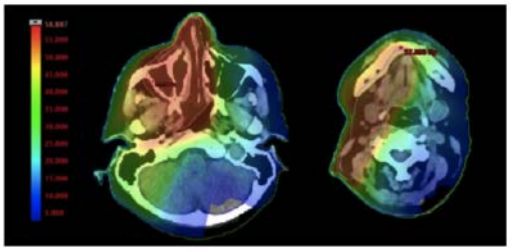

Figure 2. Target volume definition on CT scan images.

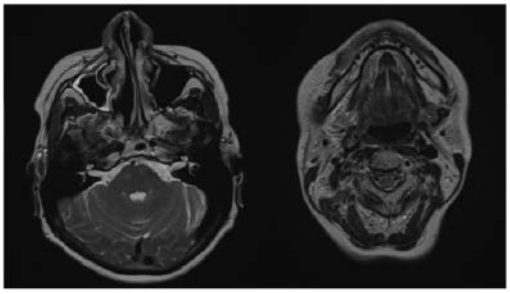

Figure 3. MRI images of the last follow-up

Figures 1-2-3.

Methods: We present a case of a 50-year-old woman with ARMS of right maxillary sinus in stage IV: T4 (6cm) N1 (ipsilateral laterocervical node) M1 (multiple bone metastasis, the most critical one of C7 vertebra with invasion of spinal canal) (Figure 1). Initially, the patient presented with moderate pain of the right shoulder and paresthesia of the extremities that improved with administration of the analgesics. Considering rarity of the tumor, histopathological review was performed confirming the diagnosis. After the MD evaluation, due to the extent and chemosensitivity of the disease, and the paucisymptomaticity of the patient, prior chemotherapy (CT) was proposed. Sequential radiotherapy (RT) was recommended after the initial response to CT. A total of 9 cycles of CT were administered: first cycle with Vincristine-Adriamycin- Ciclofosfamide, followed by 4 cycles of Vincristin-Adriamycin-Ifosfamide and 4 cycles of Ifosfamide- Etoposide. Additionally, Denosumab was given for the bone lesions. The PET scan performed after 9 cycles of CT showed complete metabolic response of the disease and the patient was referred for exclusive RT of the primary tumor and locoregional nodes. Considering the systemic aggressiveness of the ARMS maintenance dose of Ciclofosfamide-Vinorelbin was prescribed concomitantly. The Patient received Image-guided photon-based RT with VMAT, for a total dose of 54Gy in 30 fractions (1,8Gy/fx, 5 days/week) on both primary tumor and ipsilateral neck. The target volumes were defined on pre-chemotherapy imaging (Figure 2).

Results: Both treatments were well tolerated and no Grade ≥2 toxicity was documented. Eight months after conclusion of RT and 17 months from the diagnosis, the patient is alive and in complete response on all sites of the disease (Figure 3). Currently the patient is undergoing maintenance CT and regular follow ups.

Conclusion: Adults with ARMS have a very poor prognosis due to the advanced stage of the disease at diagnosis and the high metastatic potential. A multidisciplinary approach to these patients with surgery when feasible, CT and RT is the best current therapy, though long-term survivals remain poor.

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CASE REPORT: RADICAL RADIOTHERAPY FOR 44 YEARS OLD MAN WITH SYNTOMATIC CASE REPORT: RADICAL RADIOTHERAPY FOR 44 YEARS OLD MAN WITH SYNTOMATIC

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Aim: The most common primary tumor of the spine is vertebral hemangiomas (VHs), which have a reported incidence of 10% - 27% and represent 2%-3% of all spinal tumors. VHs are generally benign hamartomatous lesions derived from proliferations of normal vascular structures. VHs are usually asymptomatic and incidentally identified on radiographs, where they often have a hallmark honeycomb pattern or coarse vertical striations. Higher-grade lesions may cause pain and rarely spinal cord compression with severe neurological deficits.

Matherials and Methods: Here we described a case of a 44 years old man, with biopsy-proven hemangioma, localized in right vertebral peduncle of 12th thoracic vertebra (T12). The patient (pt) was symptomatic for dorsal pain and hypoesthesia in the right emiarea of T12 at orthopedic examination. At MRI the lesion appeared as hyperintense formation in all RM sequences, localized in T12 peduncle, and at the sequent computed tomography (CT) was seen as an osteolytic lesion with initial endocanalar protrusion. The clinical case was discussed with the multidisciplinar team (MDT) of a National Reference Centre that gave no indication to surgery but proposed

Radioterapy.

Results: Patient underwent radical daily radiotherapy (RT) up to 36Gy in 18 fractions. Treatment was done with 7 beams IMRT plan with daily megavolt cone beam CT. At starting day pt referred for dorsal pain and we prescribed desametasone, with substantial clinical stability during treatment. Patients experimented relief from dorsal pain from 14 days after the end of the treatment. A 3 months post RT CT scan showed stable desease.

Conclusion: RT is a safe and effective treatment for vertebral hemangioma. In our case the pt experimented fast relief from pain but stable desease at imaging five months after the end of radiation therapy. Further follow up is necessary to assess imaging modifications.

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ADJUVANT AND NEOADJUVANT RADIOTHERAPY IN THE MIXOID LIPOSARCOMAS OF SOFT TISSUE OF THE LOWER LIMBS: ANALYSIS OF LOCAL CONTROL AND ACUTE TOXICITY

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Aims: Historically, amputation was once considered the standard therapy to attain local control in patients (pts) with extremity soft tissue sarcoma (STS). However, improvements in imaging, implementation of adjuvant therapy and technical advances in reconstructive surgical procedures have decreased the requirement for amputation. The primary characteristic of myxoid liposarcoma (MLPS) is high radiosensitivity. RT can be used either preoperatively or postoperatively. The main advantages of preoperative RT are reduction in the RT field and total dose (DT). Postoperative RT showed no superior benefit in terms of survival and LR compared with preoperative RT. In addition, local control is better achieved using preoperative RT. The role of chemotherapy (CT) in pts with MLPS has been discussed for different situations: as neoadjuvant for local control of primary MLPS; as adjuvant in a postoperative setting and for the treatment of metastatic MLPS. Here, we present some cases of pts affected by MLPS of the lower limbs treated in our Institution.

Methods: Between May 2019 and June 2022, 5 pts affected by MLPS of the lower limbs (3 pts grade 3 MLPS, 1 grade 2 MLPS and 1 grade 1 MLPS) underwent external radiotherapy (EBRT) in our Center. 3 pts underwent neoadjuvant EBRT with DT of 50 Gy at 2Gy per fraction, and 2 pts underwent adjuvant EBRT with DT 60 Gy at 2Gy per fraction, after negative microscopic margins resection. Only a patient received neoadjuvant concomitant CT for grade 3 and lesion with diameter >10 cm.

Results: Acute dermal toxycity was evaluted by CTCAE v.4.0 scale: G1 in 3 pts, G2 in 2. No G3 toxicty was observed. The 3 pts who underwent neoadjuvant EBRT had a 50% mean reduction of the lesion and then underwent subsequent radical surgical resection. After a mean follow up of 15 months, no pts developed local relapses or metastases. The impact of adjuvant treatments on functional impotence of the limbs was also analyzed according to the Musculoskeletal Tumor Society Rating Scale (MSTS), presenting a score of 4 in 3 pts and 5 in 2 pts.

Conclusion: Our study, with a small number of pts, allows us to affirm, in accordance with the literature, that in MLPS of the lower limbs conservative surgery followed by radiotherapy allows to obtain a satisfactory local control associated with an acceptable toxicity and that neoadjuvant RT allows instead to remove the mass with a sufficient margin of surrounding normal tissue, maximizing postoperative physical function.

P274

HIT-ART (HIGHLY TAILORED ANAL CANCER IMAGE GUIDED INTERVENTIONAL RADIOTHERAPY): RESULTS OF 10 YEAR EXPERIENCE

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Aims: The aim of this study is to investigate the outcomes in terms of overall survival (OS), local control (LC), colostomy free survival (CFS), in a cohort of patients treated with chemo radiation (CRT) followed by Interventional Radiotherapy (IRT).

Method: We retrospectively analyzed patients with histologically proven squamous anal carcinoma, treated using IMRT with curative intent, who received IRT boost following CRT. External beam radiation was delivered using IMRT technique with a SIB to deliver 45 to 55Gy in 25 fractions according to clinical stage (Table 1). Four to six weeks after the end of the CRT patients underwent clinical and imaging re-evaluation, and according to initial stage of disease and tumor response, a radiotherapy boost was administered via Image Guided Interventional Radiotherapy (IG-IRT), performing MRI with applicator on site and defining GTV on MRI imaging. After treatment patients were evaluated every 2 or 4 months for the first two years and every 6 months for the next 5 years. All patients', treatments and outcomes data were collected in an Excel™ database. The endpoints were overall survival (OS), local control (LC) and colostomy free survival (CFS). Univariate survival analysis with Kaplan-Meier curves was performed to allow between-group

comparison.

Results: 62 patients treated between January 2012 and December 2021 were included in the analysis. 69% were female, with a median age of 64.8 years (range 39.1-90). 55 were staged T2-T4 (T2 43.5%, T3 19.4%, T4 25.8%) and 42 had positive nodes. Combined RCT was administered mainly using mitomycin C and 5-fluorouracil. RT was delivered with a simultaneous-integrated boost (SIB-IMRT) with 45-55.8 Gy; After a median time of 42 days (range 9-128) a sequential boost dose was delivered in 1-2 fractions (3.50-10 Gy with a median dose of 4 Gy). OTT median was 79 days (range 19-225). The median follow-up period was 38.6 months. LC, CFS and OS at 3 and 5 years were, respectively, 84.5%, 80.4%, 87.6% and 84.5%, 63.4%, 79%. Univariated analysis showed that a boost, with a dose higher than 6 Gy, was correlated to an OS at 5 years of 100% and of 70% for lower boost doses (p= 0.04). Moreover, we verified that OS was higher in patients who had an OTT lower than 93 days. There was no correlation between outcomes and initial T stage.

Conclusions: Image Guided Interventional Radiotherapy in IGRT era has proven to be a feasible treatment option with a significant impact on outcomes.

Table 1.

Table 1 IMRT Protocol (Intensity Modulated RadioTherapy)

	N0			N +			
	T	pelvic Elective nodal	groings Elective nodal	T	N0 Elective nodal	N + < 2cm	N + > 2 cm
T1 T2 (<3cm)	45** (*1.8 Gy)	45 (*1.8Gy)	36 (*1.8Gy) (with plan 20th fx)	45 (*1,8 Gy)			
T2 (>3cm)	50** (*2 Gy)		45 (*1.8Gy)	50 (*2 Gy)	45 (*1.8 Gy)	50 (*2 Gy)	55 (*2.2 Gy)
T3-T4	55** (*2.2 Gy)		45 (*1.8Gy)	55 (*2.2 Gy)			

* 25 fractions

** for all patients, after EBRT Image Guided Interventional Radiotherapy is performed (dose prescription is based on the staging and treatment response, IRT volume is defined on MRI with applicator on site)

P275

AIRO GROUP INTERVENTIONAL: ACTIVE ITALIAN IORT CENTER

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Purpose: Check the number of radiotherapy centers that perform intraoperative radiotherapy treatments with or without a dedicated accelerator.

Method: From May to April 2022 a questionnaire of 7 questions was sent to the Italian radiotherapy centers through the AIRO; at the same time a search was carried out through the manufacturers who provided a list of centers that have dedicated linear accelerators active or not with both electrons and photons.

Results: Of the 183 centers, 31 responded (17%); from the research with the companies there are 46 dedicated accelerators currently scattered at 44 radiotherapy centers therefore it can be assumed a response of 70% of the centers with dedicated accelerators (two centers have more types of accelerators). Of the 31 responses received, it emerges that: only 2% use non-dedicated accelerators; 21 centers claim to have a dedicated accelerator (electrons 17% photons 4%); 12 centers claim to be active while another 12 are not; the most commonly treated pathology is the mammary followed by sarcomas, pancreas, rectum, gynecological and prostate; the majority of active centers perform between 20 -50 procedures per year (40%) followed by 10-20 (13%) and finally more than 50 (8%); 9 centers declare an interest in developing the method with a dedicated linear accelerator.

Conclusions: Intraoperative radiotherapy is a clinical radiotherapy practice of proven efficacy and of important multidisciplinary impact. Our research (minimal) shows that in Italy the activity is underpowered compared to both the presence of linear accelerators and to the activity in its entirety, which is aimed above all of breast cancer and that a re-evaluation and training process is necessary to reactivate the necessary evolution.

P276

THE COSMETIC OUTCOME IN EARLY BREAST CANCER TREATED WITH BREAST CONSERVATION AND INTRATRAOPERATIVE RADIOTHERAPY

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Introduction: To evaluate the cosmetic outcome of breast-conserving surgery and intraoperative radiotherapy (IORT) and identify factors which influence cosmesis.

Material and Method: A total of 162 patients with early primary breast cancer treated from Genuary 2014 to Deceber 2019 with lumpectomy and IORT (21 Gy), were subjectively assessed for cosmetic outcome by a seven-member radiation oncologist panel using clinical evaluation and the Harvard/NSABO/RTOG Breast Cosmesis Grading Scale. A written questionnaire was randomly administered to 34 patients to also obtain a self evaluation assessment of the treated breast and a subjective satisfactory judgment. Clinical follow-up were performed 45 days after IORT, 6 months after the first medical check, and thereafter every 12 months.

Results: With a median follow-up of 54 months (range: 1-98 months), 101 patients (62.3%) showed good cosmetic results, 32 patients (19.7%) fair cosmetic results and 23 patients (14.2%) excellent results. Only 6 patients (3.7%) presented poor cosmetic outcome with marked fibrosis involving more than one-quarter of the breast tissue. Good correlation and agreement were found between objective expert panel and subjective patient evaluation. No clinical factors were found to affect cosmesis negatively, in particular patients older age (<70 years, 70-80 years, and >80 years) and tumor size (<1cm, 1-2 cm) do not affect the cosmetic result.

Conclusions: These cosmetic results, combined with a low local recurrence rate, validate the operative method used.

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RADIOABLATION OF VENTRICULAR ARRHYTHMIAS: DOSIMETRIC COMPARISON BETWEEN PROTONS AND PHOTONS

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Background: Stereotactic arrhythmia radioablation (STAR) is a non-invasive treatment for patients refractory to standard antiarrhythmic therapies (AT). Proton Therapy (PT), with its physical selectivity, is expected to be more advantageous than Photon-Therapy (PhT). The first-in-man experience of PT as STAR was performed at our Institution for a case of ventricular flutter refractory to multiple AT. The patient underwent a 4D SIM-CT with/without contrast and respiratory gating. This analysis aimed to retrospectively compare the RT exposure of cardiac sub-units and the dose distribution on the target between PT and PhT in this peculiar case, evaluating the potential dosimetric benefit of PT over PhT.

Methods: In the PT plan, the arrhythmogenic zone (Target), was in the base-postero-lateral left ventricle and the entity of hearth mobility was assessed by echocardiography and cardio-CT. For the PT planning, compensation for lung and cardiac motion, led to a final planning volume of 12.58 cm^3 that was isometrically expanded +1 mm to create an ITV of 22.60 cm^3 and then a PTV of 27.69 cm^3. A single dose of 25 Gy relative biological effectiveness (RBE) was delivered through two proton beams with IMPT technique and respiratory gating. This case was retrospectively re-planned on the initial 4D SIM-CT, aiming to achieve a similar PTV coverage using VMAT PhT.

Results: In both plans, PTVs received 95% coverage of the dose homogeneously. The difference between plans was the dose received by the Organs at Risk (OaRs). PhT plan showed higher doses of OARs including cardiac sub-units (D1 descending Aorta 13 Gy Vs 5.8 Gy RBE; right atrium 8.4 Gy Vs 4.7 Gy RBE; esophagus 9.3 Vs 0.06 Gy RBE). In the PT plane, except for the D2 and D1 of the pericardium (23.1-24.9 Gy RBE), right atrium (4.3-4.7 Gy RBE), left atrium (11.6-19.0 Gy RBE), right and left ventricles (4.8-4.9 Gy RBE and 25.0-25.1 Gy RBE), all the other OaRs reported doses negligible. Both plans respected QUANTEC dose constraints for not cardiac OaRs.

Conclusions: This dosimetric analysis has shown that STAR procedure with PT, compared to highly conformal PhT plans, has the advantage to reduce the dose to OaRs including cardiac sub-units. However, in PT to avoid possible target missing it is much more important than in PhT to manage cardio-pulmonary organ motion during therapy. The use of both cardiac and respiratory gating is highly recommended to improve treatment accuracy and minimize possible side effects.

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RISK FACTORS FOR LATE VAGINAL TOXICITY AFTER EXCLUSIVE ADJUVANT BRACHYTHERAPY IN ENDOMETRIAL CANCER

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Aims: To report risk factors for late vaginal toxicity after vaginal image guided brachytherapy (IGBT) in early stage endometrial cancer (EC).

Methods: From 2014 to 2019 81 stage I-II endometrioid histology EC patients (pts) received exclusive adjuvant IGBT. According to ESGO-ESTRO-ESP guidelines 7/81 (8,64%) pts were classified as low-risk, 64/81 (79,01%) as intermediate-risk and 10/81 (12,35%) as high-intermediate-risk. The median age was 66,3 years (40-87 years). All pts underwent Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy, 44 pts (54,32%) with nodes dissection and 37 pts (45,68%) without nodes dissection. IGBT with a GammaMed high dose rate remote afterloading, using a single channel vaginal cylinder CTbased planning, was performed. The upper half of vagina (median 4,5cm) was treated. The median total vaginal length was 9 (6-12cm). The fractio-

nation was A: 25 Gy in 5 fractions (fr) of 5 Gy (64,2%), B: 30 Gy in 5 fr of 6 Gy (22,22%) and C: 21 Gy in 3 fr of 7 Gy (13,58%). The dose was prescribed to 0,3-0,5 cm deph of the applicator. Bladder, rectum, sigma and small bowel were considered organ at risk. Dose constraints to 2cc of bladder and rectum were 80% and 70% of the prescribed dose respectively. D90 of CTV>100% of the prescribed dose was achieved in 74% of cases. Vaginal toxicity was graded according to CTCAE 5.0 scale. Late vaginal toxicity was evaluated against age, number of nodes removed, fractionation and vaginal length by Fisher extact test. The Kaplan-Meier method was utilized to estimate rates of tumor control and survival.

Results: The median follow-up was 59,4 months (23-125 months). Cumulative late vaginal toxicity was observed in 11/81 (13,58%) pts: 1,92% G1 and 3,84% G2 in the group A (52 pts); 27,8% G1 and 11,11% G2 in the group B (18 pts); 9,09% G2 in the group C (11 pts). No ≥ G3 adverse events were recorded. Univariate analysis showed that fractionation dose (p=0.002), >12 nodes removed (p=0.008) and vaginal length (p=0.02) ≤7cm were significantly correlated with late vaginal toxicity but not age. The 5-year overall survival, local control and disease free survival were 97,5%, 94,6% and 91,8% respectively.

Conclusions: The fractionation scheme of 30 Gy in 5 fr, >12 nodes removed and vaginal length (≤7cm) resulted in higher rates of toxicity. No grade ≥3 adverse events were observed. Our data suggest that adjuvant IGBT is well tolerated with good clinical outcomes mainly in group A.

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ORIFICE (INTERVENTIONAL RADIOTHERAPY FOR FACE AESTHETIC PRESERVATION): RESULTS OF INTERDISCIPLINARY TRIAL OF INTERSTITIAL INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) FOR PERIORIFICIAL FACE CANCER

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Background: Periorificial face skin cancers (PFC), defined as both squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) arising around the eyelids, the nose vestibule and the lips, has very high incidence rates worldwide. Aim of our retrospective analysis, focusing on local control (LC) and patients' degree of satisfaction for the cosmetic outcome, is to present the results of a single institution series of patients affected by PFC and treated by interventional radiotherapy (brachytherapy, IRT).

Methods: We retrospectively evaluated H&N cancer patients, affected by PFCs who were treated at our Interventional Oncology Center (IOC) with interstitial IRT from 2012 to 2021 with doses and volumes specific for each subsite considered.

Results: We report the results of 40 patients affected by PFC and treated by HDR interstitial IRT. The median follow-up was 24 months. The actuarial 3-years LC was 94%. No G3-4 Toxicity is reported. Regarding patients' satisfaction we obtained a 93% of patients satisfied and only 7% of the patients were not completely satisfied with the final cosmetic result.

Conclusions: Interstitial HDR IRT could be an effective therapeutic option by providing an adequate disease control and preventing from potentially disfiguring surgical approaches. Larger cohort and standardized prospective studies are warranted to confirm the available evidence.

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EVALUATION OF DEEP-LEARNING AUTO-SEGMENTATION METHODS IN ENDOMETRIAL CANCER INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY)

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Aims: Contouring of organs-at-risk (OARs) and target volumes is an essential step in endovaginal interventional radiotherapy (IRT, also called brachytherapy) treatment planning. Auto-segmentation algorithms, including atlas-based methods and deep-learning algorithms based, have the potential to reduce inter-and intra-observer variability and speed up the contouring process. This study evaluated existing standard quantitative geometric measures using atlas-based and deep-learning auto-segmentation methods for OARs and target volume in patients underwent to adjuvant endovaginal IRT for endometrial cancer.

Methods: MIM v. 7.1.5 (MIM Software Inc., Cleveland, OH), installed on a workstation with Intel Xeon 2274 CPU and 16 GB RAM, was used. A total of 10 patients with endometrial cancer who underwent com-

puted tomography (CT-based) interventional radiotherapy were included in this study. Planning CT data were acquired on Optima CT 580 (GE, General Electric) system set on helical scan mode. CT images were reconstructed using a matrix size of 512 × 512 and thickness of 0.625 mm. The planning CT volumes of involved patients for the first and second IRT treatment fraction were collected. Rectum, bladder, small bowel and clinical target volumes (CTV, the upper 3 cm of the vagina) were manually contoured on each CT. An ad hoc workflow was optimized in MIM in order to perform a rigid registration followed by a deformable registration and the subsequent automatic creation of the region of interests (ROIs) on the second CT. The manual ROIs were therefore compared to the automatic ROIs with the use of the Dice Similarity Coefficient (DSC: $(2|A \cap B|/|A|+|B|)$. It is generally accepted that a value of DSC > 0.7 represents excellent agreement.

Results: Among all structures, the best results were obtained for bladder segmentation with median DSC of 89%. Automatic segmentation also achieved a good result for CTV (median DSC 79%). The most inferior segmentation accuracies were observed on the segmentations of rectum and small bowel (DSC = 68%, DSC = 30%, respectively).

Conclusions: We presented a deep learning-based method using MIM v.7.1.5 architecture to automatically segment the target volumes and OARs in the planning CT images for endometrial cancer IRT. Quantitative evaluation results showed that the proposed method could segment the CTV and bladder with relatively good accuracy.

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EVALUATION OF DEEP-LEARNING AUTO-SEGMENTATION METHODS IN CERVIX CANCER INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY)

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Aims: Contouring of organs-at-risk (OARs) and target volumes is an essential step in interventional radiotherapy (brachytherapy, IRT, BT) treatment planning. In the last decades, auto-segmentation algorithms have been developed, including atlas-based methods and deep-learning algorithms based. This study evaluated existing standard quantitative geometric measures using atlas-based and deep-learning auto-segmentation methods for OARs and target volume in the pelvis.

Method: MIM v. 7.1.5 (MIM Software Inc., Cleveland, OH), installed on a workstation with Intel Xeon 2274 CPU and 16 GB RAM, was used. A total of 23 patients with cervical cancer who underwent Magnetic resonance (1st fraction) and computed tomography (CT-based –1st, 2nd,3rd,4th fractions) IRT were included in this study. All the enrolled patients received intracavitary high-dose-rate IRT. Planning CT data were acquired on Optima CT 580 (GE, General Electric) system set on helical scan mode. CT images were reconstructed using a matrix size of 512 × 512 and thickness of 0.625 mm. The planning CT volumes of involved patients for the first and second IRT treatment fraction were collected. Rectum, bladder, small bowel and target volumes (high (HR) and intermediate risk (IR) clinical target volume (CTV) were manually contoured on each CT. An ad hoc workflow was optimized in MIM in order to perform a rigid registration followed by a deformable registration and the subsequent automatic creation of the region of interests (ROIs) on the second CT. The manual ROIs were therefore compared to the automatic ROIs with the use of the Dice Similarity Coefficient (DSC: $(2|A \cap B|/|A|+|B|)$ and the Jaccard Similarity Coefficient (JSC: $(|A \cap B|/|AUB|)$. It is generally accepted that a value of DSC and JSC > 0.7 represents excellent agreement.

Results: The best results were obtained for bladder segmentation with median DSC and JSC values of 82% and 70%, respectively. Automatic segmentation also achieved a good result for HR-CTV (median DSC 79% and median JSC 66%) and IR-CTV (median DSC 88% and median JSC 79%) clinical target volumes. The most inferior segmentation accuracies were observed on the segmentations of rectum and small bowel (DSC = 64%, JI = 48% and DSC = 52%, JI = 35%, respectively).

Conclusion: Quantitative evaluation results showed that the proposed method could segment the HR/IR-CTV and bladder with relatively good accuracy.

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RESULTS OF ACCELERATED INTRACAVITARY INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) SCHEDULES FOR CERVIX CANCER

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Aims: The standard of care for stage IB–IVA FIGO cervix cancer consists of chemo-radiation (CRT) followed by image-guided Interventional Radiotherapy (IG-IRT, also called brachytherapy) resulting in excellent local and pelvic control. Although the European brachytherapy group (GEC-ESTRO) has carried out an excellent job in attempting to standardize the contouring of volumes, dose reporting and dose constraints to the target and organs at risk, there is currently a heterogeneity in IRT dose prescription and timing between fractions. The aim of this study is to evaluate long-term intestinal, urinary and vaginal toxicities in patients with locally advanced cervical cancer underwent exclusive radio-chemotherapy followed by accelerated IG-IRT.

Methods: All patients underwent CRT (weekly intravenous cisplatin 40 mg/m^2, 5–6 cycles, 1 day per cycle, plus 45 Gy external-beam radiotherapy (EBRT) delivered in 1.8 Gy fractions) +/- simultaneous integrated boost on positive nodes. IG-IRT schedules was as follow:

First week
- Tuesday: MRI of the pelvis, implantation, MRI of the pelvis with applicator, MRI-planning and 1st therapy session
- Wednesday: planning computed tomography (CT) and second IRT fraction delivery

Second week
- Thursday and Friday: planning CT and third and fourth IRT fraction delivery

The total IRT dose delivered to High Risk Tumor Volume was 28Gy (Total EQD2 dose 90Gy). The primary endpoint of the study was to evaluate ≥ G3 late vaginal, gastrointestinal and genito-urinary toxicity defined as any toxicity occurring six months after completion of HDR-IRT. The CTCAE v. 5 scale was used to score the toxicity.

Results: Sixteen patients were analysed. Two, four and ten patients were Stage IIB, IIIA/B and IIIC1/2, respectively. Late vaginal toxicity was recorded in 15 patients as follow: four, six and three stenosis G1, G2 and G3, respectively; nine, two and three atrophy G1, G2 and G3 respectively; seven and one teleangectasia G1 and G2, respectively. No ≥ G3 late gastrointestinal and genito-urinary toxicity was reported.

Conclusions: In the setting of concurrent chemo-radiotherapy, an accelerated IG-IRT treatment schedules seem to be feasible and safe.

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IORT IN RECURRENT HEAD AND NECK CANCER: EXPERIENCE OF NOVARA UNIVERSITY HOSPITAL

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Aims: To report on the potential role of IORT in locally advanced patients previously treated with surgery and EBRT+/-CT.

Methods: In March 2005, a man affected by cT3N2b (TNM 2004) oral cavity G2 carcinoma, was treated with neoadjuvant radio-chemotherapy: EBRT was delivered to a total dose of 50.4 Gy on CTV volume encompassing primary tumor and bilateral neck nodes + CDDP and 5-FU for 2 cycles. After transoral tumor resection and bilateral laterocervical lymph node dissection, the patient underwent 2 other cycles of chemotherapy. Ten months after the end of radiotherapy the patient developed prelaringeal cutaneous relapse that was treated by surgical removal with a boost of 10 Gy of IORT and adjuvant EBRT 30.6 Gy (1.8 Gy/fr). In November 2020, a man affected by laryngeal carcinoma (cT3N0) was treated with type II open partial horizontal laringectomy. According to pathological report (pT2N3b), after muldisciplinary discussion, patient underwent adjuvant radiochemotherapy, 66 Gy (2 Gy/fr) on laringeal bed, 60 Gy (2 Gy/fr) on positive neck levels, and 54 Gy on bilateral neck and CDDP 100 mg/mq. Eight months after the end of adjuvant treatment the patient experienced laryngeal recurrence and total laryngectomy was performed. No other adjuvant treatments because of no residual disease and no close margins. Twelve months later, in January 2022, the patient presented with peristomal recurrence. No systemic disease at CT and MRI restaging. After multidisciplinary discussion, in February, partial cervical esophagectomy + recurrence removal and IORT was performed.

Results: Both patients received 10 Gy IORT at the 85% prescription isodose, with 6 MeV electrons on surgical bed after recurrent tumor removal; the irradiated area encompassed sites at high risk of microscopic infiltration defined by ENT surgeons and radiation oncologist. In both cases no bolus was adopted and collimators were 3-6 cm. No intraoperative complications were reported. In the first months after intraoperative irradiation, both patients were hospitalized with high grade medical assistance to avoid inflammatory and infective complications. Local or distant recurrences were observed in patient treated in 2006 and the patient is free of disease after 204 months follow-up. The second patient experienced a local progression disease after 4 months.

Conclusions: IORT in head and neck recurrences was

feasible. In our experience, no serious adverse events were reported after the procedure.

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ADJUVANT INTERSTITIAL BRACHYTHERAPY IN UVEAL MELANOMA: A CASE REPORT

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Aims: Uveal melanoma is the most common primary intraocular tumor in adults, with an incidence of 5.1 cases per million per year. Extrascleral extension is rare but possible and associated with increased risk of local recurrence, metastasis, and death. Orbital exenteration and adjuvant radiotherapy remain the mainstay of treatment for extensive melanoma invading the orbit. We present a case report of choroidal melanoma with orbital invasion in a 82 year woman treated with adjuvant high dose rate brachytherapy (HDR_BT), after surgical excision.

Material and Methods: In 2018, a 82-year-old woman underwent an orbital exenteration for a choroidal melanoma with massive extrascleral extention (pT4e) followed, 1 month after surgery, by adjuvant interstitial brachytherapy of the orbit. Brachytherapy catheters were implanted intraoperatively and under general anesthesia.A marking pen was used to define the cutaneous orbital entry wounds. Typical spacing between each catheter was1-cm spanning the orbital circumference. Transcutaneous incisions were performed, then brachytherapy catheters containing metal trochars with needle tips were introduced. Each catheter had been marked to a 4 cm depth as to avoid deeper implantation. Once in place, each central metal catheter trochar was removed, and a 5.0 silk suture was used to sew the button to the skin. 7 catheters were thus implanted. After the procedure in the operating room, a 2 mm CT scan was performed and a CTV was delineated on the disease extent visible on the presurgery MRI images. A target dose of 32.5 Gy was delivered in 9 twice-daily fractions over 5 consecutive days.

Results: The treatment was well tolerated and follow-up of 44 months shows no orbital recurrence. There was no significant eyelash or eyebrow loss and the patient maintained ocular prostheses.

Conclusion: In this case report, Brachytherapy was used as an alternative to external beam radiation treatment for postenucleation orbital melanoma. Our experience reports complete local control, few side effects, and excellent cosmetic results.

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TOXICITY PROFILE OF STEREOTACTIC REIRRADIATION: RESULTS FROM PHASE I DOSE ESCALATION STUDY (DESTROY-1)

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Aims: To report the toxicity profile of a dose escalation study (Destroy-1) investigating the stereotactic radiotherapy (SBRT) retreatment (re-RT) of recurrences occurring later than 4 months after in-field radiation (RT).

Methods: In the frame of Destroy-1 trial, a phase I dose-escalation multiarm stereotactic radiotherapy (SBRT) clinical study, two arms (d) and (e) were conceived for re-RT of recurrence following prior in-field RT and were differentiated as follows: recurrences pre-irradiated with doses >60 Gy or recurrences in locations with previous small intestinal irradiation were recruited in arm (d), whereas recurrences in sites receiving a prior RT dose less than 60 Gy were recruited in arm (e). The total dose was escalated up to 45 Gy (arm d) or 50 Gy (arm e) through 6 levels, respectively (Table 1). Each cohort was evaluated for dose-limiting toxicity (DLT) and consisted of 6 patients; if one of the patients experienced a DLT, the cohort was expanded to 12 patients. DLT was defined as any radiation-related > Grade 3 toxicity (RTOG criteria) occurring within 6 months from SBRT. Adverse events occurring later than 6 months after SBRT were described as late toxicities, but were not considered in DLT evaluation.

Results: 117 lesions (41 lesions in the (d) arm and 76 in the (e) arm) accounting for 93 consecutive patients (M/F: 53/40; median age: 67 years; range 44-89) were treated from September 2004 to May 2022. About 92.5% of the patients had an ECOG performance status between 0 and 1, with coronary disease being the most frequent comorbidity (62.5%). Most patients had a primary lung (16.1%), pancreatic (12.9%) or prostate cancer (12.9%). The most common re-RT sites were pelvis (42.7%), thorax (28.2%) and abdomen (23.9%), with nodal recurrences accounting for the bulk of the lesions (59%). Median GTV was 8.9cc (0.35-146.9) and median PTV was 31.8cc

(4.1-236.0). Median follow up was 17 months (1-143). There was no acute toxicity above G2, and there was just one late toxicity >G2, consisting in a G4 soft tissue toxicity (abscess) in the pelvic area. More details on dose-level accrual and toxicity profile are shown in Table 1. Local control at 1-, 2- and 5-years was 93.0%, 76.0% and 67.1% respectively; while Overall Survival at 1-, 2- and 5-years was 81.5%, 66.1% and 27.6% respectively.

Conclusion: Retreatment of recurrence with Stereotactic radiotherapy seems to be highly feasible in terms of toxicity profile. The end of the study is awaited in order to draw definite conclusions about the safety and efficacy of SBRT re-RT.

Table 1. Dose levels accrual and toxicity profile.

DOSE LEVEL (Gy)	N° lesions	N° lesions de-escalated from superior level	Arm d: recurrences pre-irradiated with doses >60 Gy or recurrences in locations with previous small intestinal irradiation													
			Acute Toxicity							Late Toxicity						
			Upper GI		Lower GI		Skin		GU	Lung fibrosis	Lower GI		Lung fibrosis		Soft Tissue	
			G1	G2	G1	G2	G1	G2	G1	G1	G1	G2	G1	G2	G1-G2	G3-G4
20	6	1	3	1	0	0	0	0	0	0	0	0	0	0	0	0
25	6	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0
30	18	5	2	0	2	2	0	0	0	0	1	0	0	1	0	1
35	17	4	1	0	1	0	1	0	1	1	0	0	0	0	0	0
40	22	3	2	0	0	0	0	0	0	0	0	0	0	1	0	0
45	7	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0

DOSE LEVEL (Gy)	N° lesions	N° lesions de-escalated from superior level	Arm e: recurrences in sites receiving a prior RT dose < 60 Gy													
			Acute Toxicity							Late Toxicity						
			Upper GI		Lower GI		Skin		GU	Lung fibrosis	Lower GI		Lung fibrosis		Soft Tissue	
			G1	G2	G1	G2	G1	G2	G1	G1	G1	G2	G1	G2	G1-G2	G3-G4
25	4	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
30	9	2	1	0	0	0	0	0	0	0	0	0	0	0	1	0
35	10	0	1	0	0	0	0	0	0	0	0	0	1	1	0	0
40	11	1	1	1	1	0	0	1	0	0	0	0	1	0	0	0
45	6	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
50	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0

Legend: GI: gastrointestinal toxicity; GU genitourinary toxicity

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STEREOTACTIC RADIATION THERAPY FOR OLIGOMETASTATIC ESOPHAGOGASTRIC ADENOCARCINOMA. CLINICAL RESULTS AND PROGNOSTIC FACTORS

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Aims: The aim of this study was to evaluate clinical results and prognostic factors in a cohort of patient with oligometastatic esophagogastric adenocarcinoma treated with SRT.

Method: The study included patients affected by 1 to 3 metastases treated with SRT from 2013 to 2021. Local control (LC), overall survival (OS) and progression free survival (PFS) were evaluated. We also estimated time to polymetastatic dissemination (TTPD) in patients experiencing a further disease progression and time to systemic therapy change/initiation (TTS).

Table 1. Patient and primary disease characteristics.

Characteristics	Individuals	Percentage
Gender		
Male	12	21.82%
Female	43	78.18%
Presence of Comorbidities		
Yes	41	74.55%
No	14	25.45%
PS		
0	31	56.36%
1	24	43.64%
Smokers		
Active	9	16.36%
Ex	21	38.18%
Never	25	45.46%
Primary tumor site		
Stomach	22	40%
Gastroesophageal junction	18	32.73%
Esophagus	15	27.27%
Type of Adenocarcinoma		
Tubular Type	18	32.73%
Others	37	67.27%
Neoadjuvant systemic therapy for the primary tumor		
Yes	25	45.45%
No	30	54.55%
Neoadjuvant radiotherapy for the primary tumor		
Yes	13	23.64%
No	42	76.36%
Surgery for the primary tumor		
Yes	49	89.1%
No	6	10.9%
Adjuvant systemic therapy for the primary tumor		
Yes	15	27.27%
No	40	72.73%

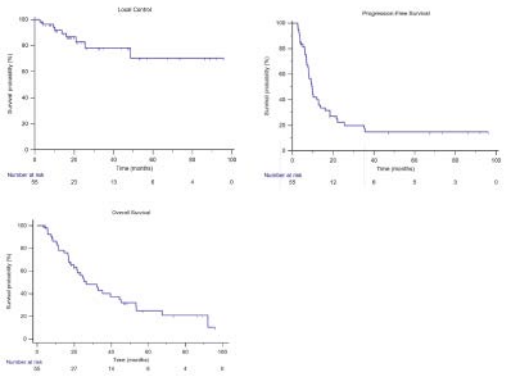

Figure 1. Kaplan Meyer curves for LC, PFS and OS.

Results: Between 2013 and 2021, 55 patients were treated with SRT on oligometastatic sites. Median age was 69 years. Primary tumor, patients and oligometastatic disease characteristics are shown in Tables 1 and 2. We observed 21 complete response (CR); 24 partial response (PR); 8 stable disease (SD) and 2 progressive disease (PD). Median follow-up was 20 months. Nine patients had local progression, median LC was not reached. 1 and 3 years LC was respectively 92% and 78%. Forty-one

patients experienced further distant disease progression, median PFS was 9.7 months, 1 and 3 years PFS was respectively 40% and 15%. Thirty-four patients died, median OS was 26.6 months, 1 and 3 years OS was respectively 78% and 40% (Figure 1).

Table 2. Oligometastatic disease characteristics.

Characteristics	Individuals	Percentage
Imaging		
CT scan only	13	23.64%
CT scan+other	42	76.36%
Disease Free Interval	493 days (median)	0-2497 (range)
Oligometastatic Type		
De novo synchronous	4	7.27%
De novo metachronous oligorecurrence	26	47.27%
Repeat oligoregurrence	7	12.73%
Repeat oligoprogression	1	1.82%
Induced oligorecurrence	13	23.64%
Induced oligopersistence	3	5.45%
Induced oligoprogression	1	1.82%
Timing of metastases		
Synchronous	10	18.18%
Metachronous	45	81.82%
Number of irradiated lesions		
1	36	65.45%
2	13	23.64%
3	6	10.91%
Location of irradiated lesions		
Lung	13	23.64%
Brain	2	3.64%
Liver	14	25.45%
Adrenal gland	1	1.82%
Nodes	22	40
Lung+Node	1	1.82%
Adrenal gland+Node	2	3.63%
SRT BED		
	78.75 (median)	45-262.5 (range)
Concomitant systemic therapy		
Yes	7	12.73%
No	48	87.27%

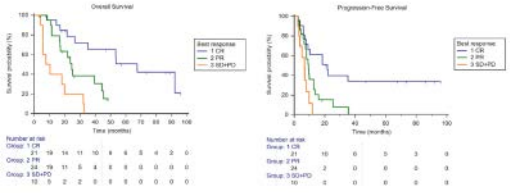

Figure 2. OS and PFS according to irradiated lesion best response at follow up.

During follow up, 24 patients changed or initiated a new systemic therapy, median TTS time was 9 months. Twenty-seven patients experienced poliprogression, 44% after 1 year and 52% after 3 years. Median TTPD was 8 months. At univariate analysis disease free interval, timing of metastases, performance status (PS) and local response (LR) influenced PFS. The best LR was related with prolonged PFS on multivariate analysis: CR vs PR+SD+PD (HR 0.36 95%CI 0.17-0.76 p=0.008) and SD+PD vs CR+PR (HR 2.36, 95%CI 1.02-5.59; p=0.04). Also timing of metastases (synchronous vs metachronous: HR 3.07, 95%CI 1.50-6.26; p=0.002) and PS (ECOG 1 vs 0: HR 2.10, 95% CI 1.10-3.97; p=0.02) were confirmed in multivariate analysis. LR and BED >75 Gy correlated with OS at univariate analysis; only LR maintained significance at multivariate analysis (p<0.0001) (Figure 2).

Conclusions: SRT represents a valid treatment for oligometastatic esophagogastric adenocarcinoma, with promising LC and OS at 3 years. CR correlated with PFS and OS, while metachronous metastasis and a good PS correlated with a better PFS. Future studies are needed to study the integration between SRT and systemic therapies.

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TOXICITY PROFILE OF STEREOTACTIC BOOST FOLLOWING PRIOR RADIOTHERAPY: RESULTS FROM PHASE I DOSE ESCALATION STUDY (DESTROY-1)

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Aims: To report the toxicity profile of a dose escalation study (Destroy-1) investigating stereotactic radiotherapy (SBRT) boost administered within 4 months of the previous conventionally fractionated radiotherapy (RT).

Methods: In the frame of Destroy-1 trial, a phase I dose-escalation multiarm stereotactic radiotherapy (SBRT) clinical study, two arms (f) and (g) were conceived for studying the optimal dose of a stereotactic boost following prior in-field RT. The 2 arms were differentiated as follows: patients receiving a boost after a prior RT dose ≤50 Gy (arm f) or after a prior RT dose >50 Gy (arm g); moreover, the total dose was escalated up to 35 Gy (arm f) or 30 Gy (arm g) through 3 levels, respectively (Table 1). Each cohort was evaluated for dose-limiting toxicity (DLT) and consisted of 6 patients; if one of the patients experienced a DLT, the cohort was expanded to 12 patients. DLT was defined as any radiation-related > Grade 3 toxicity (RTOG criteria) occurring within 6 months from SBRT. Adverse events occurring later than 6 months after SBRT were described as late toxicities, but

were not considered in DLT evaluation.

Results: 69 lesions (41 lesions in the (f) arm and 28 in the (g) arm) accounting for 57 consecutive patients (M/F: 30/27; median age: 66 years; range 43-84) were treated from July 2005 to April 2018. About 96.5% of the patients had an ECOG performance status between 0 and 1, with the most common comorbidity being coronary disease (80.6%). Most patients had a primary lung (28.1%) and breast cancer (12.3%). The most common boost sites were the pelvis (34.8%) and thorax (52.2%), with the majority of lesions being nodal metastases (52.2%). The median GTV was 9.5cc (0.1-99.7) and the median PTV was 26.8cc (1.5-281.2). Median follow up was 17 months (3-124); no acute toxicity above G2 was recorded, while only two late toxicities > G2 were recorded: one G3 intestinal bleeding and one G3 bowel stenosis. More details on dose-level accrual and toxicity profile are shown in Table 1. Local control at 1-, 2- and 5-years was 93.0%, 76.0% and 67.1% respectively; while overall survival at 1-, 2- and 5-years was 91.8%, 74.2% and 53.9% respectively.

Conclusion: Stereotactic boost within 4 months of previous RT seems to be feasible with a safe toxicity profile. The end of the study is awaited in order to draw definite conclusions about the safety and efficacy of SBRT boost.

Table 1.

DOSE LEVEL (Gy)	N° lesions	N° lesions De-escalated from superior level	Arm f: boost after a prior RT dose ≤50 Gy																		
			Acute Toxicity							Late Toxicity											
			Upper GI		Lower GI		Skin		GU	Lung fibrosis	Hematology	Lung fibrosis	Xerostomia	Skin	Lower GI			GU	Neuro-toxicity		
			G1	G2	G1	G2	G2	G3	G1	G1	G1	G1	G1	G1	G2	G1	G2	G3	G2	G3	
25	10	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	13	1	0	0	0	0	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0
30	18	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0
		Arm g: boost after a prior RT dose >50 Gy																			
DOSE LEVEL (Gy)	N° lesions	N° lesions De-escalated from superior level	Acute Toxicity							Late toxicity											
			Upper GI		Lower GI		Skin		GU	Lung fibrosis	Hematology	Lung fibrosis	Xerostomia	Skin	Lower GI			GU	Neuro-toxicity		
			G1	G2	G1	G2	G2	G3	G1	G1	G1	G1	G1	G1	G2	G1	G2	G3	G2	G3	
30	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
32	6	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
34	19	0	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0

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PSMA-PET GUIDED STEREOTACTIC BORY RADIOTHERAPY FOR BONE OLIGORECURRENT CASTRATION SENSITIVE PROSTATE CANCER

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To assess the outcomes of a cohort of bone oligometastatic prostate cancer (PC) patients treated with PSMA-PET guided stereotactic body radiotherapy (SBRT). From April 2017 to January 2021, 40 patients with oligorecurrent PC detected by PSMA-PET were treated with SBRT for bone oligometastases. Concurrent androgen deprivation therapy (ADT) was an exclusion criterion. A total of 56 PC bone oligometastases were included: 30.3% were spine-metastases, while 69.7% were non-spine metastases. Oligometastatic disease occurred after a median interval of 39 months (2-244) from the primary treatment, with a median PSA doubling time of 6.7 months (1.1-40.8). In 28 patients (70%), oligometastatic disease presented as a single lesion, two lesions in 22.5%, three lesions in 5%, four lesions in 2.5%. SBRT was delivered for a median dose of 30 Gy (24-40) in 3-5 fractions, with a median EQD2=85 Gy2 (64.3-138.9). With a median follow-up of 22 months (2-48), median local control (LC) was 18 months (2-48) with 1- and 2-years rates of 96.3% and 93.9%. The median nadir PSA (nPSA) after SBRT was 0.9 ng/ml (0.36-13.8), with 12 patients whithout a PSA drop after SBRT. Our 1- and 2-years distant progression-free survival (DPFS) rates were 45.3% and 27% for a median time interval of 9 months (3-37). At univariate analysis, a longer time to oligometastases onset favorably impacts on DPFS (p=0.0003); similarly, for lower number of treated metastases (p=0.003), lower PSA pre-SBRT (p=0.0013) and nPSA values after SBRT (p<0.0001). Also, patients who kept LC of the treated lesions maintained an advantage in terms of DPFS (p=0.017). At multivariate analysis, the lower nPSA value after SBRT remained significantly related to better DPFS rates (p=0.03). In 7 patients, a second SBRT course was proposed with concurrent ADT, while 11 patients, due to polymetastatic spread, received ADT alone, thus resulting in 1- and 2-years ADT-free survival (ADTFS) rates of 67.5% and 61.8%, for a median ADTFS time of 13.5 months (2-45). At univariate analysis, ADTFS was found to be significantly related to lower number of treated oligometastases (p=0.0001), a longer disease-free interval (p=0.0097) and lower PSA values before (p<0.0001) and after SBRT (p=0.004). At multivariate analysis, the number of treated oligometastases maintained a correlation with higher ADTFS rates (p=0.04). In our experience, PSMA-PET guided SBRT resulted in excellent results in terms of clinical outcomes and to delay the start of ADT.

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STEREOTACTIC BODY RADIOTHERAPY IN BONE OLIGOMETASTATIC HORMONE-SENSITIVE PROSTATE CANCER PATIENTS: A MULTICENTRE RETROSPECTIVE STUDY

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Aims: In oligometastatic disease, stereotactic body radiotherapy (SBRT) as metastasis direct treatment (MDT) represents a promising therapeutic option. The aim of our study is to assess the role of SBRT in hormone-sensitive prostate cancer (HSPC) patients (pts) with bone oligometastasis (BM).

Methods: This is a multicentre retrospective study of 75 HSPC pts with 94 BM treated with SBRT between October 2010 and April 2022. Primary endpoints were biochemical disease free survival (bDFS) and time to androgen deprivation therapy (ADT). Secondary endpoints were local control (LC) and toxicity. Median age was 71 yrs (range, 56-87). At the primary diagnosis, median Gleason score was 7 (range, 6-9), median PSA value 9.4 ng/ml (range, 3.1-140.9), and median stage of disease T2c and all pts were N0 and M0. Time from primary treatment to SBRT was 38 m (range, 2–131). Diagnosis of disease relapse was made with Choline-PET/CT in 70 (93%) pts and with PSMA-PET/CT and Conventional Imaging in 1 (1%) and 4 (4%) pts, respectively. Median PSA value before SBRT was 2.2 ng/ml (range 0.01–46). Twenty-five (33%) received concomitant ADT. Sixteen (21%) pts underwent SBRT for >1 synchronous lesion. BM sites were: pelvis in 51 (54%) pts, spine in 32 (34%) pts, and 11 (12%) pts in other sites. The most used fractionation regimens were: 1x24Gy (BED 81.6Gy10), 3x10Gy (BED 50 Gy10) and 5x8Gy (60Gy10). Response was assessed with PSA evaluation scheduled every 3 m during the first yr and then every 6 m. Pts with a reduction or a stability of PSA level were considered responders. Instrumental control was done in case of a PSA level increase.

Results: With a median follow-up of 24 m (range, 1-115), median bDFS from the end of SBRT was 9 m (range, 2-70). Sixty (80%) pts had a decrease of PSA level after SBRT. Of responders, 26 (42%) pts remained biochemical relapse free, the other 34 (58%) pts had a PSA increase due to in-field (7 pts) or out-field progression (27 pts). In the latter case, 8 pts underwent SBRT on a new BM and 13 pts had a systemic progression of disease and were submitted to ADT. Median time to initiation of ADT was 9 m (range, 2-70). No SBRT related acute or late > G2 toxicities were registered.

Conclusion: Our experience shows that SBRT in HSPC with BM can achieve high rates of LC with an excellent risk-benefit profile. Moreover, SBRT confirms to delay ADT allowing to an improvement of quality of life in these subset of pts.

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STEREOTACTIC BODY RADIATION THERAPY FOR LUNG AND LIVER OLIGOMETASTASES FROM BREAST CANCER: TOXICITY DATA AND PRELIMINARY RESULTS OF A PROSPECTIVE NON-RANDOMIZED PHASE II TRIAL

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Aims: We report mature toxicity data and preliminary efficacy data of a phase II non randomized trial on the use of SBRT for lung and liver oligometastases. The co-primary endpoints were local control (LC) rate and acute and late toxicity. The secondary endpoints were the evaluation of distant progression free survival (DPFS), overall survival (OS), polyprogression free survival (PoFS) and the time to start/change of systemic therapy.

Methods: Oligometastatic patients from breast cancer were treated with SBRT for up to 5 lung and/or liver lesions. Inclusion criteria were: age >18 years, ECOG 0-2, absence of life-threatening conditions, diagnosis of breast cancer, less than 5 lung/liver lesions (with a maximum diameter <5 cm), metastatic disease confined to the lungs and liver or extrapulmonary or extrahepatic disease stable or responding to systemic therapy, chemotherapy completed at least 3 weeks before treatment or started at least 2 weeks after RT, written informed consent. Various dose-fractionation schedules were used. 4D-CT scan and FDG-CTPET were acquired for simulation and fused for target definition.

Results: From 2015 to 2021, 64 patients for a total of 90 lesions were irradiated. Main patients and treatment characteristics are shown in Table 1. Treatment was well tolerated, with no G3-4 toxicities. Acute and late toxicities are shown in table 2. Median follow up was 19.4 months (range 2.6 – 73.1). LC rates were 96.2% at 1 and 3 years. Complete response, partial response and stable disease were detected in 39 (61%), 19 (30%), 6 (9%) patients, respectively. Median OS was 29.7 months. OS rates at 1 and 3 years were 86.5% and 45.8%. Median DPFS was 7.96 months, with a DPFS rate at 1 and 3 years of 35.5% and 18.77%. Median PoFS was 14.5 months, with a PoFS rate at 1 and 3 years of 64% and 23.5%.

Table 1. Patients and treatment characteristics.

Age		
Mean	61 (range 32-87)	
Performance Status (ECOG)	n	%
0	40	63%
1	21	33%
≥ 2	3	5%
Histology	n.	%
Ductal infiltrating carcinoma	53	83%
Lobular infiltrating carcinoma	5	8%
Other	6	9%
Molecular classification	n.	%
Luminal A	18	28%
Luminal B	18	28%
HER2 enriched	14	22%
Triple negative	13	20%
Disease Free Interval (years)		
Mean (range)	4.66 (0-17.8)	
Type of metastatic disease	n.	%
Synchronous	15	23%
Metachronous	49	77%
Oligometastatic status at onset of disease	n.	%
No	59	92%
Yes	5	8%
Previous local ablative treatments (LAT)	n.	%
No	44	69%
Yes	20	31%
Lines of systemic therapies before SBRT	n.	%
0	5	8%
1	23	36%
2	13	20%
≥3	23	36%
Type of oligometastases	n.	%
De-novo	15	23%
Repeat	6	10%
Induced	43	67%
N. of radiated lesions	n.	%
1	44	69%
2	15	23%
≥3	5	8%
Organs receiving SBRT	n.	%
Lung	23	36%
Liver	40	63%
Both	1	2%
Number of organs receiving SBRT	n.	%
1	63	98%
2	1	2%
Disease extra SBRT target	n.	%
Yes	23	36%
No	41	64%
Concomitant systemic therapy	n.	%
Yes	54	84%
No	10	16%
BED		
Mean	139.983	
Max	262.5	
Min	100	
Subsequent systemic therapy	n.	%
Yes	41	64%
No	23	36%

Table 2. Acute and late toxicities.

Toxicity			
	Type	n.	%
Acute toxicity		15	23%
G1			
	-Fatigue	7	11%
	-Nausea and vomiting	4	6%
	-Fever	1	2%
	-Chest pain	1	2%
	-Abdominal pain	3	5%
	-Malaise	1	2%
G2			
	-Nausea and vomiting	2	3%
Late toxicity		9	14%
G1			
	-Chest pain	2	3%
	-Chough	1	2%
	-Pneumonia	1	2%
	-Rib fracture	1	2%
	-Gastritis	1	2%
	-Gastrointestinal pain	1	2%
G2			
	-Erythema	1	2%
	-Duodenal ulcer and stenosis	1	2%

Median time to next systemic therapy was 7.9 months, with a 1-year rate of 30% and a 3-years rate of 2.5%. At univariate analysis the presence of extra-target lesions demonstrated a significant impact on OS, DPFS, PoFS; the positivity of the primary tumor to hormone receptors was associated to a longer time to next systemic therapy.

Conclusion: SBRT is an effective and safe treatment option for lung and liver oligometastatic breast cancer patients., with excellent LC, promising rates of delay in disease progression, and limited toxicity.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) AND CONCOMITANT SYSTEMIC THERAPY IN OLIGOPROGRESSIVE BREAST CANCER PATIENTS

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Aim: Breast cancer is a heterogenous disease with a deep tailoring level. Evidence are accumulating on the role of stereotactic body radiotherapy (SBRT) in the

management of oligometastatic disease. While in other histology there is a large amount of data, the evidence in oligometastatic breast cancer is limited. The aim of the present study is to show the effectiveness of SBRT in delaying the switch to a subsequent systemic treatment line in oligoprogressive breast cancer patients.

Methods: Retrospective analysis from two Institutions. The primary end-point was time to next systemic treatment (NEST). Secondary end-points were freedom from local progression (FLP), time to the polymetastatic conversion (tPMC) and overall survival (OS).

Results: One-hundred fifty-three (153) metastases in 79 oligoprogressive breast cancer patients were treated with SBRT. The median follow-up was 24 months. The median NEST was 8 months. Factors predictive of NEST at the multivariate analysis (MVA) was the number of treated oligometastases (HR 1.765, 95%CI 1.322-2.355; p=0.00). Systemic treatment after SBRT was changed in 29 patients for polymetastatic progression and in 10 patients for oligometastatic progression <6 months after SBRT. The 2-year FLP in the overall population was 86.7%. A biological effective dose (BED) >70Gy10 was associated with improved FLP (90% versus 74.2%). The median tPMC was 10 months. At the MVA the only factors significantly associated with tPMC were the number of oligometastases (HR 1.172, 95%CI 1.000-1.368; p=0.03), and the local control of the treated metastases (HR 2.726, CI95% 1.108-6.706; p=0.02).

Conclusion: SBRT can delay the switch to a subsequent systemic treatment, however patient's selection is necessary. Several predictive factors for treatment tailoring were identified.

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REIRRADIATION ON SPINE METASTASES: AN ITALIAN SURVEY ON BEHALF OF PALLIATIVE CARE AND REIRRADIATION STUDY GROUPS OF ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims: This survey derived from the collaboration between the Palliative Care and Reirradiation Study Groups of the Italian Association of Radiotherapy and Clinical Oncology (AIRO). Its aim was to obtain a real "snapshot" on the treatments of spinal metastases, focusing on re-irradiation, among radiation oncologists in Italy.

Methods: The survey was elaborated on SurveyMonkey's online interface and was sent via e-mail to all Radiation Oncologists of AIRO that were invited to anonymously fill in the electronic form within 60 days. The questionnarie was prepared by the AIRO "Palliative care" and "Reirradiation" Study Groups and it consisted of 36 questions, 19 single-choice questions, 10 multiple-choice questions and 6 open questions. The data were analyzed and represented with tables and graphs.

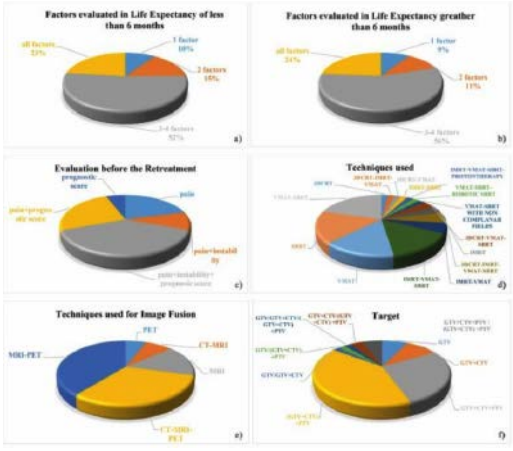

Figure 1.

Results: The survey shows that palliative radiotherapy remains a field of interest for most ROs in the Italian

centers. 3DCRT alone or in combination with other techniques is the primary choice for patients with a life expectancy of less than 6 months. For patients with a life expectancy of more than six months, there is an increased use of new technologies, such as VMAT. Factors considered for retreatment sono time between first and second treatment, dose delivered to spine metastasis and spinal cord in the first treatment, vertebral stability, symptoms, and/or performance status. The most feared complication are myelopathy followed by vertebral fracture and local recurrence. This explain an increasing focus on patient selection and the use of high technology in the treatment of metastatic patients.

Conclusions: SBRT and image-guided radiotherapy allow the administration of ablative RT doses while sparing the constraints of healthy tissue in spinal metastases. However, there is still an unclear and heterogeneous reality in the reirradiation of spinal metastases. A national registry with the aim of clarifying the most controversial aspects of vertebral metastasis retreatments will enable better management of these patients and design more targeted study designs.

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STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR SOFT-TISSUE SARCOMA (STS) LUNG OLIGOMETASTASIS: A PHASE 2 STUDY

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Aims: Lung is the most frequent site of metastasis in soft tissue sarcoma (STS) patients. Pulmonary metastasectomy is the most common treatment performed. Stereotactic body radiation therapy (SBRT) has proven to be a potential alternative to resection. We aimed to assess role of SBRT for lung metastatic patients in a prospective phase 2 study.

Methods: Adults patients with lung metastasis (LMs) up to 4, ≤5cm, unsuitable for surgery were included. Dose prescription was based on site and size: 30Gy/1fraction for peripheral lesions ≤10mm, 60 Gy/3fractions for peripheral lesions 11-20mm, 48 Gy/4fractions for peripheral lesions >20mm, and 60 Gy/8fractions for central lesions. Primary endpoint was proportion of treated lesions free from progression at 12 months. Secondary endpoints were disease free survival (DFS), overall survival(OS), and toxicity.

Results: Between March 2015, and December 2020, 44 patients for 71 LMs were enrolled. Twelve-month local control was 98.5%±1.4, reaching primary aim; median DFS time,1,2,3,4,5-year PFS rates were 12 months (95%CI 8-16 months), 50%±7.5, 19.5%±6.6, 11.7%±5.8, 11.7%±5.8, and 11.7%±5.8, respectively. Median OS time,1,2,3,4,5-year OS rates were 49 months (95%CI 24-49 months), 88.6%±4.7, 66.7±7.6, 56.8%±8.4, 53.0%±8.6, and 48.2%±9.1, respectively. Prognostic factors recorded as significantly impacting survival were age, grade of primary sarcoma, interval time from diagnosis to occurrence of LMs, and number of LMs. No severe pulmonary toxicity (grade 3-4) occurred.

Conclusions: We found a high percentage of local control and survival in almost all patients treated. Toxicities were negligibles. Well-designed randomized trials comparing surgery with SBRT for lung metastatic STS patients are needed to confirm this preliminary data.

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STEROTACTIVE ABLATIVE RADIOTHERAPY (SABR) FOR INTRA AND EXTRACRANIAL OLIGOMETASTASIS OF SMALL CELL LUNG CANCER (SCLC): A RETROSPECTIVE, MULTICENTRIC, EXPLORATIVE STUDY

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Aims: SCLC is the most aggressive lung cancer histology with a 5-year overall survival (OS) <10%. At the diagnosis, almost two-thirds of the SCLC an Extended Disease (ED) presentation. Recently two randomized studies (CASPIAN and ImPower133) demonstrated an OS improvement, when immunotherapy (IT) was prescribed as maintenance therapy after standard chemotherapy (CHT). To date, SABR has had a limited indication in managing metastatic SCLC, although recent reports proposed it as a valid treatment option in selected patients. We propose a retrospective multicentric analysis of patients treated with SABR for oligometastatic SCLC.

Method: Data of 34 patients affected by oligometastatic-SCLC treated with SABR (maximum 8 fractions and a minimum dose/fraction of 5 Gy) between 2017 and 2021 in six Italian Centers were collected. The primary endpoint was to describe the pattern of care with SABR of oligometastatic SCLC, while secondary endpoint was the analysis of OS. A descriptive analysis of patient and treatment characteristics was elaborated. A Kaplan-Meyer's Curve for OS was calculated.

Results: The median age was 65 years (range 36-79), and all but one had Performance Status (PS) 0 or 1. Seventeen patients presented ED at diagnosis. The first line treatment was concomitant radiochemotherapy (CHT-RT) in 11.8%, sequential CHT-RT in 35.3%, CHT alone in 32.4% and CHT-IT in 17.6%. Sixty-one metastatic lesions were treated with SABR; 37 (60.6%) in brain, 9 (14.7%) in lung, 3 (5.1%) in liver, 1 (1.6%) in lymph nodes, 5 (8.2%) in bones and 6 (9.8%) in adrenal gland. At the moment of data collection 35.3% of patients were still alive while 64.7% died due to disease. After a median follow up of 23.8 months, median OS, 2 years OS and 5 years OS were 22.8 months, 50% and 9%, respectively. No statistically significant difference resulted between Limited Disease (LD) and ED at diagnosis in terms of OS.

Conclusions: Despite the retrospective nature of the study, the results show a longer OS in our population compared to data shown in CASPIAN and ImPower133 trials. This result suggests that the local control achieved with SABR could translate in a better OS in SCLC. Moreover, this population represents a selected sub-group of oligometastatic SCLC patients with an unexpected OS that could be interpreted as a different clinical presentation and biology compared to plurimetastatic disease.

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THE ROLE OF MAGNETIC RESONANCE-GUIDED STEREOTACTIC BODY RADIATION THERAPY (MRGSBRT) IN THE TREATMENT OF LYMPH NODE OLIGOMETASTASES

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Aims: Lymph nodes represent a common site of metastatic tumor spread and Stereotactic Body Radiotherapy (SBRT) is becoming a widely used technique for ablative metastasis-directed treatments. Recently, hybrid linear accelerators with low-field integrated MR systems (MR-Linac) have introduced the option of real-time treatment plan optimization on a patient-specific basis (online adaptive radiotherapy), by utilizing the exceptional soft tissue contrast resolution offered by magnetic resonance (MR) imaging and state-of-the-art online gating methods. The aim of this retrospective, single center study was to define efficacy and feasibility of Magnetic Resonance-guided Stereotactic Body Radiation Therapy (MRgSBRT) in the oncological treatment framework in a case series of oligometastatic patients with lymph node metastases.

Method: We retrospectively collected data from oligometastatic patients (≤ 5 metastases) with lymph node metastases from miscellaneous primary tumors, treated with MRgSBRT. In-field local progression-free survival (LPFS) and progression-free survival (PFS) at 12 months, as well as overall-survival (OS) at 24 months were calculated using the Kaplan Meier analysis. The objective response rate (ORR) included complete response (CR) and partial response (PR). We observed clinical benefit (CB) if ORR or stable disease (SD) were acquired. Treatment safety was evaluated in terms of acute and chronic toxicity rates assessed according to the Common Terminology Criteria for Adverse Events version 5.0 (CTCAE v5) scale.

Results: Seventy lesions from 46 enrolled patients treated with MRgSBRT at our center from September 2017 to April 2021 were selected for analysis. Patient and treatment characteristics are summarized in Table 1. The treatments of 27 lesions (38.5%) were delivered using the online adaptive feature, whereas the breath-hold technique was applied in 24 lesions (34.2%). We observed complete and partial responses in 42 (60%) and 7 (10%) lesions, respectively, while SD was detected in 6 (8.57%) lesions, for an overall CB rate of 78.5%. During a median follow-up period of 15 months (range 2-51 months), the 12-month actuarial LPFS and PFS were 81.1% and 31.3% respectively, while OS at 24 months was 97%. No acute nor late grade ≥3 toxicities were reported.

Conclusions: Our study confirms that MRgSBRT is an efficient and safe local ablative technique that allows for PTV dose-escalation while sparing OARs in treatment of lymph node metastases.

Table 1.

	N. (%)
Patients	46 (100)
Lesions	70 (100)
Age, yrs	
Median (range)	69 (41-84)
ECOG Performance Status	
0-1	44 (95.7)
2	2 (4.3)
Primary tumor	
Ovary	27 (38.6%)
Prostate	18 (25.7%)
Cervix	4 (5.7%)
Lung	3 (4.3%)
Other	18 (25.7%)
PTV	
Median, range (cc)	5 (1.2-66.2)
Total dose, Gy	
Median (range)	40 (15-50)
Dmean $BED_{\alpha/\beta\ 10}$	
Median (range)	71.8 (19.5-130.2)
Dose/fraction, Gy	
Median (range)	8 (4-10)
Gating	
Breath-hold inspiration	24 (34.3%)
Free breathing	46 (65.7%)
Adaptive online RT	
Number of lesions	27 (38.6%)

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PATTERNS OF FAILURE AFTER STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LIVER METASTASES: IMPACT OF LOCAL CONTROL

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Aims: Surgical resection of liver metastases (LM) may be feasible for only 30% of patients due to unfavourable location, disease burden or comorbidities. There's evidence of excellent local control (LC) and low toxicity in patients treated with stereotactic radiotherapy (SBRT) but data on global disease control are scarce. The aim of this preliminary analysis was to assess patterns of failure in a cohort of patients treated with SBRT to LM.

Method: Data from patients treated between 2018 and 2020 at a single Institution with SBRT to LM were collected. Patients received an EQD2 of at least 50 Gy (α/β=10) as per ESTRO consensus. Failure patterns after SBRT defined as local relapse (LR), intrahepatic relapse (out of field, IHR) and extrahepatic relapse (EHR), as well as Local Control (LC) and Overall Survival (OS) rates, were evaluated.

Results: Forty-three patients with liver-only metastatic disease received SBRT. Most common primary tumors were breast (n=18.42%) and colon (n=10.23%) cancer. SBRT was performed using Cyberknife real-time tumor tracking (n=30,70%) or abdominal compression-assisted VMAT (n=13.30%) delivering 35-60 Gy in 3-5 fractions, corresponding to median EQD2 of 94 (50-150) Gy. Twelve (28%) patients were chemotherapy-naïve, while the remaining patients received 1 (20,46%), 2 (5,12%) or ≥3 (6,14%) chemotherapy lines. Median follow-up was 12 months. Patterns of failure are reported in Table 1. One-year OS was 87%. At multivariate analysis LC was significantly correlated with EQD2≥94Gy (p=0.009) and ≥3 chemotherapy lines (p=0.04). IHR and EHR were significantly associated with local failure (p=0.0013) and intrahepatic progression (p=0.03), respectively. A significant correlation between OS and local relapse was shown (p=0.026).

Conclusions: In our experience, improved LC using high BED in non-heavily pretreated patients was correlated to reduced risk of IHR and to improved OS. IHR was the most common mode of failure in patients treated with SBRT for LM and was correlated with further extrahepatic progression. Our findings suggest that IHR may result from uncontrolled macroscopic LM rather than ubiquitous micrometastatic dissemination, and preceed further systemic spread at distant sites. Our findings support the use of SBRT as an efficient tool to block stepwise metastatic spread from uncontrolled isolated LM to liver, and from liver to distant site, thus extending global disease control.

Table 1.

Patterns of failure after SBRT: 39 patients had progressed after 1 year. 34 of them had IHR, either isolated (2), or in combination with LR (12), EHR (11) or both (9). 5 patients manifested EHR only.

	+LR	+IHR	+EHR	+IHR +EHR
LR	0	12	0	9
IHR	12	2	11	/
EHR	0	11	5	/
IHR +EHR	9	/	/	/

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STEREOTACTIC BODY RE-IRRADIATION FOR GYNECOLOGICAL CANCER: OUTCOMES AND TOXICITY

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Aims: To report the toxicity profile, local control (LC) rate, and Quality of life (QoL) data in patients suffering from recurrent gynecological cancer undergoing stereobody radiotherapy (SBRT) retreatment.

Methods: Data from patient folders were retrospectively collected, focusing in particular on primary, previous systemic therapies and previous radiotherapy treatments. Concerning SBRT, the total dose (5 daily fractions) was delivered with a linear accelerator using VMAT technique. Acute and late toxicities were assessed by the RTOG/EORTC scales. The quality of life (QoL) was evaluated according to the CLAS 1 (fatigue), 2 (energy level) and 3 (daily activities) scales.

Results: 23 patients (median age 67 years, range 48-80) bearing 27 lesions were treated from December 2006 to August 2021. The majority of patients had ovarian (39.1%) and endometrial cancer (39.1%) as primary tumour. The most used SBRT schedules were 30 Gy (37.0%), 35 Gy (29.6%) and 40 Gy (29.0%). More details are shown in Table 1. With a median follow up of 18 months (range 1-95), no patients presented acute or late toxicities higher than grade 2, except for one case of

grade 4 bone toxicity (fracture) 26 months after SBRT. This patient was treated for a sacral lesion with 40 Gy, having previously received 45 Gy on the pelvic nodal area. One year- and 2 years-LC were 84.0% and 76.3% respectively, while the 1 year- and 2 years-OS were 81.6% in both cases. Overall clinical response rate was 70.8% with a complete response rate of 65.4%. Regarding QoL, no statistically significative difference was found between the baseline and follow-up values: the median CLAS1, CLAS2 and CLAS3 was 6 (range 4-10) at baseline for each category, and still 6 (range 3-10) one month after SBRT.

Conclusion. According to this preliminary experience, in-site SBRT retreatment for recurrent gynaecological cancer could be considered a quite feasible and safe treatment without any short term QoL impairment.

Table 1. Patients and treatment characteristics.

Patients	
23	
Lesions	
27	
ECOG	***n(%)***
0-1	22 (95.8)
2	1 (4.2)
Comorbidities	***n(%)***
Cardiovascular disease	15 (68.2)
Diabetes	1 (4.5)
Second tumour	1 (4.5)
Other	5 (22.8)
Site	***n(%)***
Nodal lesions	16 (59.3)
Parenchymal lesions	10 (37.0)
Bone lesions	1 (3.7)
SBRT schedule	***n(%)***
25Gy in 5 fractions	1 (3.7)
30Gy in 5 fractions	10 (37.0)
35Gy in 5 fractions	8 (29.6)
40Gy in 5 fractions	7 (29.0)
45Gy in 5 fractions	1 (3.7)

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STEREOTACTIC RE-IRRADIATION OF RELAPSED INTRACRANIC LESIONS: A MONOINSTITUTIONAL EXPERIENCE

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Aims: A second course of radiotherapy (reirradiation) is more often used as a salvage treatment for recurrent primary brain tumors or metastases (mts). We report the experience of our Institute with reirradiation with stereotactic radiotherapy in pts with intracranial recurrence.

Methods: From 1/2018-1/2022, 160 lesions in 41 patients (pts) were re-irradiated with robotic SRT (Cyberknife®,CK). Primary tumor was NSCLS for 13 pts, breast cancer for 12, glioblastoma for 5, meningioma for 3, hemangiopericytoma for 2, oligodendroglioma for 2, pituitary adenoma for 2 pts, prostate cancer and melanoma for 1 patient. Previous RT on the same volume was performed with: Gamma Knife in 10 pts, whole-brain RT in 10, CK in 9, post-operative IMRT in 5, VMAT SRT in 4, and post-operative 3D-CRT in 3 pts. Median time from previous RT was 13 (3-378) months. Eight pts had ≥2 previous treatments. Median GTV was 6.9 (0.02-78.32) cc. Median PTV was 12 (0.07-136.9) cc. Median prescribed dose was 30 (21-35) Gy in 1-5 fractions, at a median isodose of 70 (69-80)%. Prophylactic corticosteroid therapy was prescribed to all pts.

Results: Median follow-up after re-irradiation was 10 (0-38.5) months. SRT was delivered on a median number of 1 (1-24) lesions; 8 pts were treated on >5 lesions simultaneously (from 6 to 24 lesions). Acute toxicity was G2 headache in 3 pts: (with GTV>1cc or >3 lesions), treated by increasing the dose of corticosteroids. Radionecrosis occurred in 3 pts: 1 patient (GTV 1.38 cc) underwent 2 previous VMAT SRT and presented seizures, 1 patient (GTV 0.49 cc) underwent 1 previous VMAT SRT and presented headache and 1 patient (GTV 5.54 cc) underwent previous GK and CK and was asymptomatic. Local control, evaluable in 34 pts, was: complete response (RC) in 2 patients, partial response (PR) in 18 pts, stable disease (SD) in 6 pts and progressive disease (PD) in 8 pts. Six- and 12 month overall survival were 81% and 57.9% respectively (see Figure 1). Six- and 12-month local relapse-free survival were 73.5%, 57.3%. Six- and 12-month intracranial recurrence-free survival was 68.7% and 57.2%.

Conclusions: SRT reirradiation of brain recurrent disease is effective with responses in 76.5% of pts. Three

cases of radionecrosis were recorded: an accurate patient selection is warranted in order to avoid toxicity and a longer follow-up is needed to confirm these results.

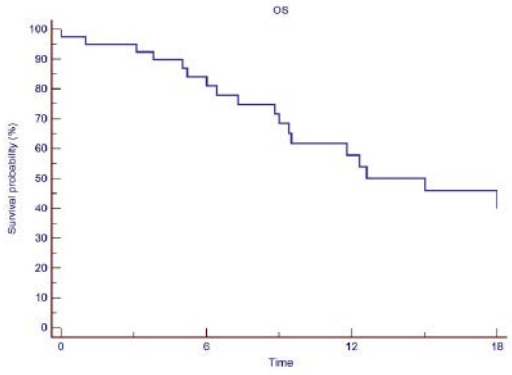

Figure 1.

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SALVAGE ROBOTIC SBRT FOR PROSTATE/PROSTATE-BED RELAPSE AFTER PREVIOUS RT

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Aims: There is no standard management of prostate cancer (PCa) local relapse after radiotherapy, due to a high risk of local side effects. The aim of this study is to report our experience with the use of high-precision stereotactic body radiation therapy (SBRT) for the treatment of local relapse, evaluating efficacy and toxicity.

Methods: This retrospective study includes 20 pts, treated between December 2018 and March 2022, with imaging and/or biopsy-proven recurrent PCa. Median interval from previous radical/salvage external beam RT was 89 (17-209) months. Salvage SBRT was delivered with CyberKnife (Accuray, Sunnyvalle, CA) image-guided radiation therapy to the prostate/prostate bed. Median dose prescribed was 35 (25-35) Gy in 5 fractions. The 2-Gy equivalent dose (EQD2) was 85 Gy (for $\alpha/\beta = 1.5$) or 63.23 Gy (for $\alpha/\beta = 4.2$). Ten pts were treated with androgen deprivation therapy at the time of re-RT. Previous RT EQD2 dose was 74 Gy (64.8-90.6). Toxicity assessment was based on CTCAE version 5.0 criteria.

Results: Median follow-up was 18 (2.4-38.2) months. Median pre-SBRT prostate specific antigen (PSA) of 2.10 ng/mL decreased to 0.09 ng/mL at the last examination in non-relapsed patients. Kaplan Meier estimates of biochemical recurrence free survival (bRFS) was 94.1% at 6 months, 86.3% at 12 months and 65.7% at 24 months. At the time of the analysis, one patient experienced local relapse (Figure 1) and a single bone metastases, another patient had a nodal relapse and underwent another SBRT, and 3 patients had biochemical relapse only. No grade (G)≥ 3 acute toxicity was observed; acute G2 genitourinary (GU) events were 10%. Among 18 patients, who had a follow up longer than 6 months, 3 patients reported late GU toxicity ≥G3. One patient presented G2 edema of the lower limbs. No acute or late rectal toxicity was registered.

Conclusions: SBRT re-RT for isolated local PCa recurrences appears clinically feasible and safe. Although longer follow-up is required before definitive statements on late toxicities and efficacy, in our series we observed favorable PSA and local control, with low GU and no rectal toxicity.

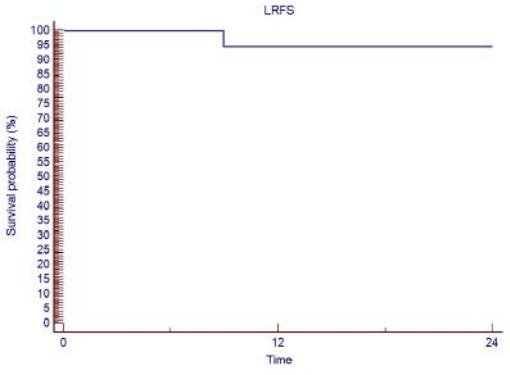

Figure 1.

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REPEATED MAGNETIC RESONANCE IMAGE-GUIDED STEREOTACTIC BODY RADIOTHERAPY (MRIG-RESBRT) FOR OLIGOMETASTATIC PATIENTS: REPAIR, A MONO-INSTITUTIONAL RETROSPECTIVE STUDY

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Aims: Stereotactic body radiotherapy (SBRT) is an effective local treatment option in the management of oligometastatic disease. Several studies have demonstrated its role in the improvement of disease control and survival outcomes. Moreover, the introduction of hybrid magnetic resonance imaging SBRT allows real-time tumor tracking (cine-MRI) and to perform online adaptive radiotherapy (oART). The aim of this study is to retrospectively evaluate the efficacy and toxicity profile of Magnetic Resonance image-guided repeated SBRT (MRIg-reSBRT) for oligomestatic pts.

Method: We retrospectively enrolled pts with in-field or closely adjacent out-of-field (between 2 and 5 cm) lung and liver metastasis or perihepatic abdominal carcinosis candidate to MRIg-reSBRT. Second SBRT doses were determined based on the tumor size and distance to Organs at Risks (OaRs). Acute and late toxicities were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) scale version 5. Overall response rate (ORR= partial and complete response) and clinical benefit (CB= ORR and stable disease) were assessed at 12 months from the end of reSBRT. Progression-free survival (PFS) and overall-survival (OS) at 12 months were calculated using the Kaplan Meier analysis.

Results: From July 2019 to January 2020 26 pts completed prescribed course of MRIg-reSBRT for 37 metastatic lesions, with a mean interval of 8,61 months (range 2-28) from the first SBRT. Table summarize pts characteristic. For 7 liver lesions we performed oART. 25 lesions (67,5%) were treated in breath hold inspiration. The mean prescribed dose of the first treatment was 43,1 Gy (range 24-50Gy, BEDα/β10=80) and 46,4 Gy (range 35-50Gy, BEDα/β10=88) for abdominal and lung, respectively. For reSBRT the mean prescribed dose was 41,3 Gy (range 16-50Gy, BEDα/β10=75) and 42,5Gy (range 35-50Gy, BED α/β10=80) for abdominal and lung, respectively. The average mean liver dose was 4 Gy and 3 Gy for the first SBRT and re-SBRT, respectively. Instead, for the first SBRT the mean lung V20 was 1,66% besides for re-SBRT was 0,81%. At a median follow-up from reSBRT of 10,7 months (range 2-34), we did not report acute and late toxicities >1. At 1 year OS and PFS was 73,08% and 50% respectively, with an ORR and CB were both 54%.

Conclusions: This retrospective analysis suggests that MRIg-reSBRT is a safe and a valid integrated option in a multi-treatment strategy for oligoprogression and/or oligorecurrence metastatic disease.

Table 1.

Characteristic	n (%)
Age, median (range)	69 (46-87)
Sex	
Male	12 (46,2%)
Female	14 (53,8%)
Primitive site of tumor	
Colorectal cancer	6 (23,1%)
Gynecologist cancer (ovary, uterine)	11 (42,30%)
Hepatocellular carcinoma	2 (7,7%)
Others	7 (26,9%)
Oligometastatic disease classification	
Metachronous oligorecurrence	1(3,8%)
Metachronous oligoprogression	19(73%)
Induced oligiopersistence	4(15,4%)
Induced oligoperistence	2(7,7%)
Irradiated metastatic Lesion reSBRT	37
Lung	12 (32,4%)
Liver	18 (48,6%)
Perihepatic abdominal carcinosis	7(19%)
In field/near field lesion	5 (13.5%)/32(86.4%)
Gating treatment for lesion	
Breath hold inspiration	19 (73%)
Free breathing	
Online adaptive	
lesion	7(18,9%)
n° fraction, mean (range)	5 (19%)3 (2-5)
PTV volume (cm3), mean (range)	13,8(1,4-55,5)
PTV Dose I SBRT liver or Perihepatic abdominal carcinosis, median dose (range)	43,1 (24-50), 80
PTV Dose reSBRT liver or Perihepatic abdominal carcinosis, median dose (range), BED $_{\alpha/\beta 10}$	41,3 Gy (16-50), 75
PTV Dose I SBRT Lung (Gy), mean dose (range), BED $_{\alpha/\beta 10}$	46,4 (35-50), 88
PTV Dose reSBRT Lung (Gy) mean dose (range), BED $_{\alpha/\beta 10}$	42,5 (35-50), 80
Liver dose reSBRT (Gy), mean dose (range), EQD2	3Gy (1–7Gy), 2,65
V20 Lungs reSBRT (%), mean (range)	0,81% (0,19-3,33)
Acute Toxicity	
GI Grade 1	0
Pulmonary Grade	0
Late Toxicity	
GI Grade 1	0
Pulmonary Grade 1	2 (7,6%)

P301

OUTCOMES AND TOXICITIES OF RE-IRRADIATION FOR GYNEACOLOGICAL CANCER: A SYSTEMATIC REVIEW ON BEHALF OF RE-IRRADIATION AND GYNEACOLOGICAL WORKING GROUP OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims: The aim of this study was to provide a literature review on the efficacy and safety of reirradiation(re-I) of locoregional recurrences in gynaecological malignancies.

*Methods:*A computerized literature search was performed in 4 electronic databases from 1993 to 2020 and full-text screening without duplicate citations was carried out. Random-effects models were used due to great subjectivity given the lack of related control groups in the non-comparative studies and a tendency towards high heterogeneity (examined by the Cochran Q chi-square test and the I2 statistic). To determine the pooled ≥G3 acute and late toxicity rate, locoregional control (LC), and overall survival (OS), an established meta-analysis technique over single and multi-arm studies was performed.

Results: Out of 178 articles, only those with outcomes limited to re-I patients and specific radiotherapy techniques were included and twenty articles accounting for 876 patients met the inclusion criteria.Outcomes were evaluable for 543 patients.The median 2-5y OS and 1y-2y-3y LC were reported in Table 1. Subgroup analyses were performed highlighting moderate to high heterogeneity among studies (range I20-100%).BT (Brachytherapy) showed a 2y OS of 62.8% (95% CI: 0.538 to 0.704, P=0.5034) and 5y OS of 44% (95% CI: 0.322 to 0.545, P=0.8572) with 1y-2y-3y LC of 76.3% (95%CI: 0.647 to 0.844, P=0.0626), 51.4% n(95%CI:P=0.9074), and 50.3% (0.353 to 0.627, P=0.9084), respectively. Using SBRT (Stereotactic Body Radiation Therapy) re-I technique, the pooled 2y OS was 49.5% (95%CI: 0.183 to 0.716, P =0.7567). CT (Chemotherapy) does not improve SBRT outcome. Data on toxicity were analysed in 18 studies with 382 pts [BT (282 pts), EBRT+BT(11 pts),EBRT+SBRT+CT (15 pts), SBRT+CT (19pts), SBRT(41pts), EBRT+CT+ Surgery+IORT (Intra-Operative Radiation Therapy) (14 pts)]. Re-I with BT technique showed pooled G3 late toxicities of 5 % (95%CI: -0.0682 to 0.177, P=0.9913), whereas using SBRT re-I, G3 late toxicities was 4.16% (95%CI: -0.192 to 0.271,P=0.9604).Only for BT and SBRT G3 late toxicities data correlated to re-I dose were obtained resulting higher when BED10 ≥100 Gy.

Conclusions: Results of the present AIRO review on re-I of gynaecological cancer revealed a large heterogeneity among studies, but promising results in terms of safety and feasibility.Among analyzed re-I techniques,BT resulted the best kind of radiation therapy delivery in terms of clinical outcome and comparable to the SBRT technique in terms of toxicities.

Table 1. Outcomes according to investigated techniques and number of patients included in the review.

Technique (n pz)	2y-OS (%)	5y-OS(%)	1y-LC(%)	2y-LC(%)	3y-LC (%)
BT (344)	60	43	73.7	53	53
EBRT+BT (56)	n.a	66.5	n.a	n.a	61.7
EBRT+SBRT+CT (15)	60	42	n.a	n.a	n.a
SBRT+CT (19)	37.3	n.a	47	n.a	n.a
SBRT (41)	50	n.a	100	63	66,7
EBRT+CT+Surgery +IORT (68)	9	7	30	n.a	n.a

n.a: not available

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SABR ON MEDIASTINAL AND HILAR LYMPHO ANDENOPHATY FROM LUNG TUMOR

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Aims: Stereotactic Ablative Radiotherapy (SABR) is the standard of care for early-stage, medically inoperable, non-small cell lung cancer (NSCLC). Mediastinal and hilar lymphadenopathy (MHL) is a frequent pattern of cancer spread, especially in primary lung malignancies. Recently, there has been interest in the application of SABR for MHL, especially in the oligometastatic setting, to improve local control (LC) and achieve shorter treatment durations to minimize systemic treatment breaks. Initial reports of severe toxicity after SABR to central lung tumors raised safety concerns with high SABR doses in that area. Limited data exist on the safety and efficacy of SABR for MHL. Aims of this retrospective study is to evaluate clinical outcomes and toxicities of SABR on MHL.

Methods: From July 2009 to December 2020 we have treated 56 MHL from lung tumor in 48 patients. The median age was 69 years (range: 54-90 years) and the Performance Status was ≤2. Forty-six MHL were from NSCLC, 4 were from SCLC and 6 from others histologies. The state of patients at moment of treatment was classified as oligorecurrent (52%), oligoprogression (27%), oligometastatic (9%) and oligopersistent (12%). The schedule of treatment most represented was 48 Gy in 8 fractions (range 23-60 Gy in 1-8 fractions). The medium BED10 was 86 Gy (range 48-120 Gy). The medium volume of MHL treated was 10 cc (range 0.74-60.3 cc).

Results: The Local control was 89%, with rates at 1 and 3 years of 89% and 83% respectively. The loco Regional Nodal Control was 78%, with rates at 1 and 3 years of 81% and 70% respectively. The Distant Nodal Control was 91%, with rates at 1 and 3 years of 92% and 88% respectively. The Distant Metastasis Free Survival was 32 % with rates at 1 and 3 years of 49% and 36% respectively. The rates of Overall Survival at 1 and 3 years were 66% and 35% respectively. At univariate analysis, the volume of CTV (volume > 10 cc) was associated with worst DMFS (P = 0,0281) and OS (P = 0,0015). Treatment was well tolerated. The acute and late toxicities was < Grade 2 .

Conclusions: SABR on MHL appears to be a safe technique for the local control of isolated nodal disease with limited toxicity.

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RE-SBRT: IS IT AN OPTION FOR THE TREATMENT OF IN FIELD RECURRENT LUNG CANCER?

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Aims: Stereotactic Body Radiation Therapy (SBRT) is the radiotherapy of choice for primary, recurrent, or secondary lung lesions. SBRT is a technique able to give an optimal distribution of ablative dose to the tumor volume sparing healthy tissues. Aim of our study is to analyze clinical outcomes and toxicities of a retreatment of recurrent in field lung lesions previous treated by SBRT with a new cycle of SBRT.

Methods: From April 2011 to October 2021 we have re-treated with SBRT 16 in field recurrent lesion previous irradiated with SBRT. The median age of patients was 75 (range 68-87 year) and the Performace Status was <1. We had various primary tumors (60% lung, 33% colon rectal and 7% gynecological). The schedule of first treatment most represented was 30 Gy in 1 fractions (range 23-54 Gy in 1-5 fractions). The medium BED10 was 116,36 Gy (range 75,9-120 Gy). The medium EQD2(10) was 102,6 Gy (range 63,25-126 Gy). For the second course of SBRT the schedule of treatment most represented was 45 Gy in 3 fractions (range 30-54 Gy in 3-10 fractions). The medium BED10 was 81 Gy (range 56,25-151,2 Gy). The medium EQD2(10) was 71,67 Gy (range 40-126 Gy). The medium cumulative BED10 of two treatments was 200 Gy (125-240) and EQD2(10) was 173 Gy (range: 140-200Gy). The medium volume of lesions of first treatment was 13 cc (range 5,07-34,28 cc) and of second treatment was 28,61 cc (range 8,9-64,9 cc).

Results: The Local Control (LC) was 44%, with rates at 1- and 2 years of 43% and 43% respectively. The Progression Free Survival (PFS) was 19% with rates of rates at 1- and 2 years of 40% and 27% respectively. The rates of Disease Specific Survival (DSS) at 1- and 2 years were 87% and 66% respectively. The rates of Overall Survival (OS) at 1- and 2 years were 87% and 66% respectively. At univariate analysis we have found that cumulative BED10 >200Gy was statistically correlated with LC (P = 0,0131), DSS (P = 0,0464) and PFS (P = 0,0284). Furthermore, the cumulative EQD2(10) >173Gy was statistically correlated with LC (P = 0,0113) and PFS (P = 0,0214). In terms of acute toxicities we did not recorded acute toxicities ≥3. In terms of late toxicities we have had two case of grade 3 (in form of dyspnea and pain), in the other cases we have recorded toxicities <2.

Conclusions: The use of SBRT on in field recurrent lung lesion already irradiated by SBRT is possible, feasible and acceptable.

P304

STEREOTACTIC RADIOTHERAPY FOR LUNG METASTASES IN PATIENTS WITH OLIGOMETASTATIC DISEASE (OMD): A RETROSPECTIVE ANALYSIS OF OUTCOME ACCORDING TO THE NEW ESTRO-EORTC OMD CLASSIFICATION

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Aims: Stereotactic body radiotherapy (SBRT) is a safe treatment modality, and it is effective to treat limited-size lesions thanks to highly conformal radiation technique. SBRT is associated with high local control rate with a low toxicity level. The aim of this study was to evaluate local control and overall survival in patients with OMD and lung lesions treated with SBRT.

Methods: Consecutive patients with OMD and lung lesions treated with Linac-based SBRT at a single radiotherapy center were included in this retrospective analysis. Data collected included diagnosis, patient demographics, number of previous lines of cytotoxic treatment, dosimetric and survival data. Local control (LC) and overall survival (OS) were estimated "per lesion" using the Kaplan-Meier method from the day of SBRT start to the time of event occurrence or last patient's follow-up.

Results: From June 2010 to February 2022, 107 patients (63 men and 44 women, median age 70, range 10-95 years) with OMD received SBRT to 202 metastatic lung lesions from rectal (59 lesions, 29%), lung (32

lesions, 16%), colon (32 lesions, 16%), , breast (22 lesions, 11%), gynaecological (11 lesions, 5,5%), sarcoma (11 lesions, 5,5%), head and neck (10 lesions, 5%), and other tumour sites (25 lesions, 12%). In 152/202 cases, at least one line of systemic therapy had been administered before SBRT. 56 (28%) lesions were de-novo oligometastases, 108 (53%) repeated, and 38 (19%) induced ones. The median follow-up time for living patients was 35 months. The 2-year local control rate was 62.7% for all treated lesions and did not significantly differ between different classes of OMD. The 2-year overall survival rate was 75.8% (59.0% de-novo, 79.6% repeated, 91.0% induced, $p<0.01$).

Conclusions: In this retrospective single-centre series, SBRT was effective in patients with lung oligometastases and provided long-term local control in most cases. Survival probability after SBRT varied accordingly to the ESTRO-EORTC OMD classes, with induced OMD having the best prognosis.

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STEREOTACTIC BODY RADIOTHERAPY IN OLIGOMETASTATIC PROSTATE CANCER: PRELIMINARY RESULTS OF A RETROSPECTIVE ANALYSIS

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Aims: To assess the outcomes of oligometastatic prostate cancer treated with stereotactic body radiotherapy (SBRT).

Methods: We retrospectively analyzed all consecutive patients treated with SBRT at our center between February 2017 and February 2022. Inclusion criteria were: oligometastatic/oligoprogressive/oligorecurrent disease, previous radical treatment for prostate cancer, radiological diagnosis of recurrence by MRI or PSMA/choline PET/TC. Exclusion criteria were: presence of visceral metastasis, previous severe disease that did not allow SBRT delivery. SBRT schedule was defined by radiation oncologist experienced in prostate cancer treatment. SBRT was delivered by Helical Tomotherapy or Varian TrueBeam.

Results: SBRT was administer to 47 pts. Median age was 77 years (range 54-88). At first diagnosis 37/47 (79%) pts and 10/47 (21%) underwent prostatectomy and radical EBRT, respectively. Median time from primary treatment and SBRT treatment was 10 years (range: 1-24). 36/47 pts (77%) had a relapse at the lymph nodes level (26 pelvic nodes, 8 lumbo-aortic nodes and 1 mediastinic), 14/47 (13%) at bone level. SBRT was guided by PSMA PET/TC, Choline PET/TC and MRI in 29/47 (63%), 16/47 (35%) and 1/47 (2%) pts respectively. Median PSA pre-SBRT was 0,96 ng/ml. 35/47pts (75%) received hormonal therapy (HT) concomitant to SBRT, 13/47 pts (25%) underwent exclusive SBRT. The most frequent RT schedule was 35Gy/5 fractions (32/47 pts). No severe toxicities (≥G3) were detected. Median PSA nadir post-SBRT was 0,64 ng/ml. At a median follow up of 15.2 months (range:3.1-53.7), 17/47 (36%) pts presented a complete radiological response, 6/17 (35%) of these received concomitant HT during and after SBRT. 12/47 (26%) presented stable disease or partial response at re-evaluation, of these 7/12 (54%) pts received concomitant systemic treatment and 3/13 (23%) received exclusive SBRT. 12/47 (25%) pts presented progression disease (2 biochemical relapse, 11 bone and 1 node relapse), 4/11 (37%) pts presented oligoprogression disease and received further SBRT on bone lesions. 6 (13%) pts were lost at follow up. At last follow up, 43/47 pts (91.5%) were alive and 4/47 patients were deceased.

Conclusion: SBRT for oligometastatic/oligoprogressive prostate cancer patients is effective and well-tolerated. In our experience the majority of patients did not progressed after SBRT.

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SABR ON LYMPH NODES METASTATS FROM COLON RECTAL CANCER

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Aims: One of the most frequently reported tumor histology for oligometastases is colorectal cancer (CRC). Systemic therapy has been able to prolong the rates of survival in patients with stage IV colorectal cancer, increasing the relative significance of local therapy for patients with oligometastases. Aims of this study is to find predictive factors of response in terms of clinical outcomes and toxicity in patients treated on lymph node metastasis (NMs) from CRC by SABR.

Methods: From August 2011 to September 2021 we have treated 24 NMs from CRC in 19 patients. The median age of patients was 66 (46-87 years) and the Performance Status was ≤1. The state of patients at moment of treatment was classified as oligorecurrent (42%), oligoprogressive (54%) an oligoperistent (4%). Four NMs were treated in the mediastinum, 11 in the pel-

vis and 9 in the abdomen. The schedule of treatment most represented was 45 Gy in 3 fractions (range 23-60 Gy in 1-8 fractions). The medium BED10 was 87,5 Gy (range 45-112, 5 Gy). The medium volume of NMs treated was 7cc (range 0.49-21.50 cc).

Results: The median Follow-up was 20 months (0-123 months). The Local Control was 92% with rates at 1 and 3 years of 96% and 89% respectively. The loco Regional Local Control was 96% with rates at 1 and 3 years of 94% and 94% respectively. The Distant Nodal Control was 83% with rates at 1 and 3 years of 92% and 81% respectively. The Distant metastasis Free Survival was 21 % with rates at 1 and 3 years of 58% and 20% respectively. The rates of Overall Survival at 1 and 3 years were 74% and 50% respectively. At univariate analysis, the volume of CTV (volume < 7 cc) was associated with better LC (P = 0,0322). The number of metastasis >1, BED10 >87Gy, the number of systemic therapy before the treatment by SABR >4, the localization of NMS (mediastinum) were correlated with worst results in terms of DMFS (P = 0,0190; P = 0,0145; P = 0,0016; P = 0,0076 respectively). Furthermore, the number of systemic therapy before the treatment by SABR >4 and the localization of NMS (mediastinum) were correlated with worst results in terms of OS (P < 0,0001; P = 0,0150 respectively). Treatment was well tolerated. The acute toxicities was one case of dysphagia G1 and one case of death caused by esophageal bleeding, G5. We have not registered case of late toxicity.

Conclusions: SABR on NMS from CRC is able to achieve good results in terms of clinical outcomes with poor toxicity. A good selection of patients is important to obtain better results.

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PATTERN OF RECURRENCE AFTER STEREOTACTIC BODY RADIOTHERAPY OF NODAL LESIONS: A RETROSPECTIVE SINGLE-INSTITUTION ANALYSIS

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Aims: Stereotactic body radiotherapy (SBRT) is an effective treatment option for the treatment of oligometastatic disease of lymph nodes. Despite the encouraging local control rate, progression-free survival remains unfair due to relapses that might occur in the same district or at other sites. The recurrence pattern analysis after nodal SBRT in oligometastatic patients could pave the way for different strategies of therapeutic intensification.

Methods: The failure pattern of patients with nodal metastases who were recruited and treated with SBRT in the DESTROY-1 study was investigated in this single-institution, retrospective analysis. The previous SBRT treatment provided to the affected lymph nodes a total dose ranging from 20 to 50 Gy in five daily fractions. The different sites of relapse were recorded.

Results: Data on 98 patients who received SBRT on 119 nodal lesions were reviewed. The male/female ratio was 44/54 and the median age was 66 years (range: 37-87). The most represented primary cancer was gynaecological one (38.7%), followed by genitourinary cancer (16.8%). Pathologic lymph nodes were most frequently located in the thorax (36.1%) followed by the pelvis (30.2%) and the abdomen (27.7%). After SBRT the recurrences were diagnosed at imaging after a median distant metastasis-free survival (DMFS) of 11 months (range: 3-84 months). The pattern of failure was loco-regional in 56 (47.1%) and distant in 63 (52.9%) patients, respectively. The most common primary tumor in patients with loco-regional failure were gynaecological, genitourinary, and lung cancer, which were found in 23 (41%) cases, 10 (17.9%), and 9 (16%) cases, respectively. Furthermore, 23 of 56 patients who were treated and then relapsed loco-regionally had the relapse in the pelvic area. The median follow-up of the overall series was 21 months (range 6-141 months).

Conclusions: Relapses following SBRT nodal irradiation were somewhat more common in distant regions than in loco-regional sites in our study. The most common scenarios for locoregional relapse appear to be gynecological cancer and the pelvic site.

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ACUTE TOXICITY EVALUATION AFTER STEREOTACTIC BODY RADIATION THERAPY SALVAGE REIRRADIATION FOR INTRAPROSTATIC RECURRENCE

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Aims: More than 30% of patients (pts) experience biochemical failure and clinical relapse after definite radiation therapy (RT) for prostate cancer (PC). To date, androgen deprivation therapy (ADT) is the preferred treatment choice, but a re-irradiation (Re-I) could be considered. The aim of the present retrospective monocentric

study is to evaluate the acute toxicity of pts undergoing Re-I with Stereotactic Body RT (SBRT) for intraprostatic PC relapse.

Materials and Methods: All pts treated in our institute with Re-I for a intraprostatic PC relapse between January 2019 to today were analyzed. Inclusion criteria were: age >18 years; pts who underwent salvage Re-I for intraprostatic recurrence after radical RT; concurrent/adjuvant ADT to SBRT was allowed; PS 1 or 2; pts who underwent positron emission tomography (PET) and magnetic resonance imaging (MRI) for restaging. Primary endpoint is gastro-enteric (GE) and genito-urinary (GU) acute toxicity incidence according to CTCAE v.5.0 RS.

Results: From 2019 to 04/2022, 20 pts met the inclusion criteria and were enrolled. Median follow up was 12 months (range 3.5-47 months). Prescription dose was 30 Gy in five fractions in one week with external beam radiotherapy (EBRT) using Volumetric Modulated Arc Therapy (VMAT). Two pts received Re-I on entire prostatic gland while in 18 pts the target included only the macroscopic lesion detected on MRI. Median PTV was 12.9 cc (5.4 -76.3 cc). Nineteen pts received EBRT for primary treatment with a dose ranged from 57.5 to 78 Gy in 25-39 fractions, while only one patient received upfront SBRT with 30 Gy in five fractions. The median time from first treatment to relapse was 79.7 months (range 39-158 months). The recurrence after Re-I occurred in only two pts (10%) after 2 and 4 months, respectively. Both developed pelvic lymph node oligo-recurrence. Median time from Re-I to PSA nadir was 5.5 months. Regarding acute toxicity: one patient developed a G3 haematuria, 4 pts a G2 cystitis and only one patient had G2 rectal toxicity (diarrhea).

Conclusions: Although our series includes a small number of pts and the median follow up is only 1 year, we can affirm that the SBRT using VMAT for the treatment of intraprostatic relapse has shown good effectiveness with low recurrence rates and acceptable acute toxicity profile.

P309

STEREOTACTIT RADIOTHERAPY CAN ACHIEVE GOOD LOCAL CONTROL AND DEFER THE NEED FOR SYSTEMIC THERAPY IN PATIENTS WITH OLIGOMETASTATIC IODINE-REFRACTORY THYROID CANCER

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Aims: Differentiated thyroid cancer is usually associated with a good prognosis, but the development of metastases in Iodine-refractory thyroid cancer adversely affects patients' quality of life and survival. The advent of tyrosine-kinase inhibitors drugs (TKI) allowed a great improvement of patients' outcome but, in case of oligometastatic disease, a locoregional ablative approach such as Stereotactic Radiation Therapy (SRT) could effectively control tumor progression and possibly defer the need of systemic therapies.

Methods: We retrospectively analyzed patients with differentiated oligometastatic thyroid cancer treated with SRT in our Radiation Oncology Unit from 2011 to 2021.

We collected demographics and treatment-related characteristics. Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS) rates were evaluated. Patients with anaplastic histology, incomplete treatment or without follow-up information were excluded.

Results: We retrospectively analyzed a cohort of 19 patients, aged between 47 and 84 years old (median 64,1). Ten (52,6%) patients were males and 9 (47,4%) were females. A total of 56 lesions were treated: 22 were located in bones (39,3%), 19 in lymph nodes (33,9%), 7 in the brain (12,5%), 5 in the lungs (8,9%) and 3 visceral (5,4%). SRT was delivered in 1-8 fractions, with a median dose of 30Gy (range 24-60Gy). Median follow-up was 36,5 months (range 6–125 months). After SRT we observed a complete response in 29 lesions (51,8%), partial response in 17 (30,4%), stable disease in 9 (16,1%) and only 1 progressive lesion (1,8%). We observed 10 local recurrences (17,8%) with an actuarial LC of 96,1% and 92,1% at 12 and 24 months respectively, while PFS was 62,0% and 55,1% at 12 and 24 months respectively. The OS at 12, 24, 48 months was 100%, 87,4% and 80,7%, respectively. A total number of 10 patients (52,6%) underwent TKI treatment (5 Sunitinib and 5 Lenvatinib) for progressive disease: median time to first systemic treatment from SRT was 18,8 months (range 1-68 months). At the end of this analysis, 9 patients (47,4%) were still without systemic therapy, showing a good disease control after a median follow-up of 30,9 months (range 6-76).

Conclusions: In our experience, SRT yields satisfying local control rates in oligometastatic Iodine-refractory thyroid cancer, allowing for a deferral of the need for systemic therapies.

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CLINICAL OUTCOMES OF STEREOTACTIC BODY RADIATION THERAPY FOR OLIGOMETASTATIC PATIENTS WITH LYMPH NODE METASTASES FROM GYNAECOLOGICAL CANCER

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Aims: To evaluate the effect of stereotactic body radiation therapy (SBRT) on the clinical outcomes as a local treatment for lymph node metastases originating from gynecological cancer.

Methods: We retrospectively analyzed 29 lymph node metastases in 22 oligometastatic/oligoprogressive patients treated with ablative SBRT between November 2007 and October 2021 at our institution. SBRT was delivered by volumetric-modulated arc therapy (V-MAT) and Intensity-modulated radiation therapy (IMRT). All patients underwent image-guided radiotherapy (IGRT) using cone-beam computed tomography (CBCT) system as daily pre-treatment imaging. Follow-up was performed with a CT scan with contrast medium or FDG/PET-CT every three months for the first two years after SBRT and every six months afterwards. The primary endpoints were overall survival (OS), local control (LC) and progression free survival (PFS). Secondary endpoints were acute and late toxicities.

Results: Median age was 61 years (range, 47–87 years). Most common primary tumor was carcinoma of uterus (68.2%). Sixteen patients received systemic therapy before SBRT. The median Gross Tumor Volume (GTV) and the Planning Target Volume (PTV) were 5.7cm^3 (range 0.28-45.58 cm^3) and 14.31 cm^3 (range 1.61-100.35 cm^3) respectively. Median SBRT dose was 36 Gy (range 23-60 Gy). Median dose per fraction was 10Gy (range 5-30 Gy). The median survival was 20 months and the actuarial 6-months, 1-year, 2-year and 5-year OS were 100%, 85.6%, 53.5% and 19.8% respectively. 6-months, 1-year, and 2-year LC was 93.1%, 87.9% and 79.8% respectively. 6-months, 1-year, and 2-year PFS were 60.7%, 45.5% and 11.4% respectively. Clinical response after SBRT evaluated using RECIST criteria revealed completed response in 18 lesions (62%) , partial response in 8 lesions (27.5%) , stable disease in 1 lesion (3.4%) and progressive disease in 2 lesions (6.8%). The 1-year and 2-year, OS for BED<70Gy vs BED>70Gy was 74.2%, and 31% *vs* 93%, and 72% respectively (CI 95% 0,1103 to 0,9091; 0.05 p-value). The 1-year and 2-year, OS for GTV<10 cm^3 *vs* GTV>10 cm3 were 88% and 44% vs 80% and 68.6% respectively (CI 95% 0,3368 to 2,413; 0.84 p-value). Four patients experienced acute toxicities, mostly grade 1-2 of asthenia. Conclusion: Despite the limited number of patients investigated in our study, SBRT is a feasible approach for lymph node recurrence, offering excellent in-field tumor control with low toxicity profile.

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PROSPECTIVE TRIAL OF STEREOTACTIC ABLATIVE RADIOTHERAPY TO PRIMARY LOCALLY ADVANCED TUMOR IN OLIGO-METASTATIC NON SMALL CELL LUNG CANCER PATIENTS: GOOD NEWS FOR A NEW STANDARD OF CARE!

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Aims: Stereotactic Ablative Radiotherapy (SABR) has shown high rates of local control and prolonged survival in early-stage non-small cell lung cancer (NSCLC), though its role in oligometastatic disease is undefined. This study aimed to evaluate SABR as a local consolidative therapy in oligometastatic (oligoM) NSCLC patients.

Methods: In this prospective trial, we sought to evaluate SABR to primary locally advanced (LA) tumor, regional nodal and metastatic sites in oligoM NSCLC patients. Fit patients received initial systemic therapy according to driver mutations and PDL1(international guidelines). Patients without progression after front-line therapy (chemotherapy, targeted therapy and immunotherapy) were evaluated by 18F-FDG-PET/CT to receive consolidative SABR to the primary, regional nodal and all metastatic sites (≤ five lesions).

Results: Between May 2018 and December 2021, 25 oligoM NSCLC were included. Median age was 71 years (range,38-87), 17 (68%) were male and 18 (72%) had adenocarcinoma histology. The main site of metastasis was bone, adrenal gland and brain in 7 (28%), 4 (16%) and 3 (12%) patients, respectively. 15 (60%) patients received systemic front-line therapy: chemotherapy in 6 (24%), immunotherapy in 12 (48%) and a tyrosine kinase inhibitor in 3 (12%). The median administered dose to primary LA tumor was 45 Gy (range,35-50) in 5 fractions. Median follow-up achieved 12 months (range, 4-53). 3 (12%) and 7 (28%) patients developed local relapse and distant metastasis after a median time of 14 months (range,9-15) and 4 months (range,3-6), respectively. No adverse events of ≥G3 was recorded. At las follow-up 19 (94%) patients are alive, 10 (40%) discontinued first front-line therapy and started second-line therapy.

Conclusions: The use of SABR on primary LA tumor in oligoM NSCLC patients was well tolerated and showed favorable clinical outcomes regarding second line therapy-free survival and overall survival. Considering the results of other prospective trials, SABR to primary LA tumor should be included as standard of care in oligoM NSCLC patients.

P312

THE IMPACT OF STEREOTACTIC RADIOTHERAPY ON SURVIVAL OF OLIGOPROGRESSIVE METASTASES FROM RENAL CELL CARCINOMA

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Renal cell carcinoma represents 80-90% of all kidney tumor and 3–5% of all adult cancers. About 15-25% of operated patients will develop distant metastases after primary treatment. Ablative radiotherapy seems to be a valid alternative to more invasive metastasectomy, even in the setting of oligoprogressive disease, defined as the progression of few isolated sites during systemic therapy. Our aim was to analyze the control of disease, survival, and toxicity of a group of kidney cancer patients treated with SRT on cranial and extracranial oligoprogressive metastases. We analyzed patients affected by kidney cancer treated with SRT on oligoprogressive site of disease during systemic treatment. A maximum of 5 sites of oligoprogression in up to 2 organs was allowed for SRT. All cases were presented to and approved by the multidisciplinary oncologic team of our Institution. Indication to treat sites of oligoprogression was generally reserved to patients unfit for the intensification or switch of systemic treatment or affected by an indolent disease characterized by a long disease free interval. End points of the present study were overall survival (OS) and progression-free survival (PFS). We included 74 oligoprogressive metastases and 57 treatments in 44 patients. Site of treated SRT was intracranial for 26 (35.1%) lesions, and extracranial for in 48 (64.9%) patients. Most common site of body metastases were lung (21 metastases, 28.3%), bone (10 metastases, 13.5%), and liver (6 metastases, 8.1%). Median follow-up was 19.0 months (0.5 – 100.2). Median OS was 36.3 months with a 1- and 2-year rate of 79.2% (95%CI 63.8 – 88.6), and 57.3% (95%CI 39.5 – 71.7). Repeated SRT on oligoprogressions was associated with improved OS (p=0.009). Median PFS was 9.8 months, and rates at 1 and 2 years were 43.2% (95%CI 29.8 – 55.9) and 25.8% (95%CI 14.2 – 39.1). According to our analysis SRT represents an effective treatment for oligoprogressive renal cell carcinoma, with the potential to ablate isolated foci of disease resistant to on-going systemic therapy.

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FIVE-FRACTION STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES: A SINGLE-INSTITUTION EXPERIENCE ON DIFFERENT DOSE SCHEDULES

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Introduction: The most common intracranial neoplasm diagnosed in adults are brain metastases (BrM). The benefit in terms of clinical control and toxicity for stereotactic radiotherapy (SRT)has been investigated for patients with low load of brain metastases. Aim of this single-institution experience was to investigate the best dose schedule for five-fraction stereotactic radiotherapy (FFSRT).

Methods: A retrospective analysis of patients treated for BrM with different dose schedules of FFSRT was performed. Local Control and clinical outcomes were evaluated with Magnetic resonance imaging (MRI) at 3, 6 and 9 months. Toxicity data were also collected.

Results: A total of 41 patients treated from November 2016 to September 2020 were enrolled in the analysis. Non Small Cell Lung cancer (51,2%) and breast cancer (24,3%) represented the most frequent primitive tumors. Treatment was performed on 5 consecutive days with prescribed dose ranging from 30 to 40 Gy, prescribed to the 95% isodose line that covered at least 98% of the GTV. Statistically significant differences (p=0.025) with higher LC control rates for dose schedules > 6Gy for fractions. Toxicity rates were not found to be higher than G1.

Conclusion: The results of this retrospective analysis suggest that FFSRT for BrM seems to be safe and feasible. Our results also underline that a total dose lower than 30 Gy in 5 fractions should not be used due to the expected minor LC.

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MRI GUIDED RADIOTHERAPY (MRGRT) IN RECURRENT RECTAL CANCER: A MONOISTITUTIONAL EXPERIENCE

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Aims: Recurrent rectal cancer (RRC) is a complex clinical condition requiring multidisciplinary treatment. Potential therapeutic strategies include surgery, chemotherapy (CHT) and radiotherapy (RT) and the treatment decision must take into account previous treatments. Reirradiation of an area where tissue has already received radiation is also a challenging decision given the risk related to cumulative toxicity to organs at risk (OARs). The advantages of magnetic resonance guided RT (MRgRT) consisting of innovative adaptive online RT (OART), gating and OARs-sparing solutions could be advantageous in this patient setting. The aim of this study is to evaluate the feasibility of reirradiation of RRC by MRgRT technique.

Method: Data from RRC patients treated with MRgRT from February 2017 to May 2022 were retrospectively analysed. All patients underwent surgery, RT in both adjuvant and/or neoadjuvant settings combined or not with CHT. RRC was diagnosed by MRI or CT examination and classified according to the Royal Marsden classification. The decision to refer patients for RT was made after discussion at the multidisciplinary tumour board. The RT dose was decided based on clinical judgement, on the recurrence localization and the cumulative dose received to the OARs. In particular, the following were taken into account: a bladder point cumulative equivalent dose of 2Gy/fraction (EQD2) up to 120 Gy, a cumulative rectal EQD2 of 70-100 Gy and for the femoral heads a cumulative biological equivalent dose (BED) 90-100 Gy. Acute toxicity was graded according to the Common Terminology Criteria for Adverse Events v.5.0 scale.

Results: The data of 9 RRC patients are shown in Table 1. The median time to re-irradiation was 25 (range 4-121) months. In 7 (77,8%) cases RT retreatment was performed with concomitant fluoropyrimidine-based CHT to enhance radiosensitivity. The most frequently used fractionation was 39.6 Gy delivered in 22 fractions. The CTV to PTV margins used were 0.5 cm and the treatment was carried out under free-breathing conditions by direct gating with continuous online cine MRI. All patients completed the RT course without interruption, mild acute G1 diarrhea was reported in 4 (44,5%) cases. No patients underwent surgery after retreatment.

Conclusions: The treatment of RRC with MRgRT technique is feasible and well tolerated. Future prospective studies proposing treatment protocols are needed to standardize the treatment workflow in this patients' setting.

Table 1.

	N (%)
Median age at RCC treatment (range)	65 (62-79)
Pathological stage at diagnosis	
1	2 (22,2)
2	2 (22,2)
3	4 (44,5)
4	1 (11,1)
RRC classification	
anterior below peritoneal reflection	3 (33,3)
posterior	2 (22,2)
lateral	2 (22,2)
central	2 (22,2)
First treatment delivered dose on GTV Dose/fractionation (Gray)	
36/1,8	1 (11,1)
50,4 /1,8	1 (11,1)
54 /1,8	5 (55,6)
25/5	1 (11,1)
55/2,2	1 (11,1)
Retreatment delivered dose Dose/fractionation (Gray)	
39,6/1,8	5 (55,6)
30,6/1,8	1 (11,1)
40,8/1,2 bid	2 (22,2)
30/6	1 (11,1)

P315

THE ROLE OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOPROGRESSIVE METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) DURING ARTA: A RETROSPECTIVE MONOCENTRIC STUDY

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Aims: This monocentric, single-arm, retrospective study investigated the use of Stereotactic Body Radiotherapy (SBRT) in patients (pts) with metastatic castration resistant prostate cancer (mCRPC) who experienced oligoprogression during androgen receptor targeted agents (ARTAs) therapy, namely enzalutamide or abiraterone. The aim of our study was to evaluate the role of SBRT as metastasis-directed therapy to postpone the current systemic treatment.

Method: We retrospectively evaluated all mCRPC patients treated with ARTAs (abiraterone 1 g per day plus prednisone 10 mg/day or enzalutamide 160 mg per day), between december 2016 and january 2022. All pts experienced an oligoprogression (defined as the appearance and/or the progression of 1 up to 5 bone or nodal metastases) during ARTA, had ECOG Performance Status of 0-1, and received a SBRT upon oligoprogressive metastatic

sites, preserving ARTA. SBRT was delivered under image guidance (IGRT). The dose selection was based on the volume and localization of oligometastases. Pts were treated with a total dose of 30 Gy up to 37,5 Gy in five fractions with a biologically effective dose (BED) of at least 90 Gy using an 3 Gy α/β ratio. New SBRT upon new metastatic sites was also permitted. Pts showing visceral metastases or receiving palliative radiotherapy were excluded. Progressive disease at > 5 metastatic sites, or the appearance of visceral metastases led to a change of the systemic treatment. In a median follow up of 50 months, we evaluated the 3-years survival rate of pts on treatment with ARTA. We also assessed the SBRT local control of disease as a secondary endpoint.

Results: We analyzed data from 24 pts (2 pts were lost-to-follow-up). The 3-years survival rate was 92%, (22/24 pts); 3-years survival rate of pts who were still on treatment with ARTAs was 50%. 16 of 24 patients had performed imaging control after a single course of SBRT: 35% experienced a complete response, 12% partial response, 47% stable disease, and 6% progressive disease. The overall response rate was 47%, while clinical benefit was 94%. No ≥G2 adverse events related to SBRT were recorded.

Conclusions: SBRT in oligoprogressive metastatic sites during ARTAs resulted in a feasible and effective treatment to prolong overall survival, delaying the start of next-line systemic treatment in mCRPC. Longer follow-up and further prospective studies are necessary to confirm our preliminary results.

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1.5T MR-GUIDED DAILY-ADAPTED STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE RE-IRRADIATION: A PRELIMINARY REPORT OF TOXICITY AND CLINICAL OUTCOMES

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Aims: Prostate re-irradiation is an attractive treatment option in the case of local relapse after previous radiotherapy, either in the definitive or in the post-operative setting. In this scenario, the introduction of MR-linacs may represent a helpful tool to improve the accuracy and precision of the treatment.

Method: This study reports the preliminary data of a cohort of 22 patients treated with 1.5T MR-Linacs for prostate or prostate bed re-irradiation. Toxicity was prospectively assessed and collected according to CTCAE v5.0. Survival endpoints were measured using Kaplan-Meier method.

Results: From October 2019 to October 2021, 22 patients received 1.5T MR-guided stereotactic body radiotherapy for prostate or prostate-bed re-irradiation. In 12 cases SBRT was delivered to the prostate, in 10 to the prostate bed. The median time to re-RT was 72 months (range, 12-1460). SBRT was delivered concurrently with ADT in 4 cases. Acute toxicity was: for GU G1 in 11/22 and G2 in 4/22; for GI G1 in 7/22, G2 in 4/22. With a median follow-up of 8 months (3-21), late G1 and G2 GU events were respectively 11/22 and 4/22. Regarding GI toxicity, G1 were 6/22, while G2 3/22. No acute/late G≥3 GI/GU events occurred. All patients are alive. The median PSA-nadir was 0.49 ng/ml (0.08-5.26 ng/ml), for 1-year BRFS and DPFS rates of 85.9%. Twenty patients remained free from ADT with 1-year ADT-free survival rates of 91.3%.

Conclusions: Our experience supports the use of MR-linacs for prostate or prostate bed re-irradiation as a feasible and safe treatment option with minimal toxicity and encouraging results in terms of clinical outcomes.

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REDUCTION OF INTER-OBSERVER DIFFERENCES IN THE DELINEATION OF THE TARGET IN SPINAL METASTASES STEREOTACTIC BODY RADIOTHERAPY (SBRT) USING AN AUTOMATIC CONTOURING DEDICATED SYSTEM

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Aims: Approximately one third of cancer patients will develop spinal metastases, which can be associated with back pain, neurological symptoms and deterioration in performance status. Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) have been offered in clinical practice mainly for the management of oligometastatic and oligoprogressive patients, allowing the prescription of high total dose delivered in one or few sessions to small target volumes, minimizing the dose exposure of normal tissues. Due to the high delivered doses and the proximity of critical organs at risk (OAR) such as the spinal cord, the correct definition of the treatment volume becomes even more important in SBRT treatment, thus making it necessary to standardize the method of target definition and contouring, through the adoption of specific guidelines and specific automatic contouring tools. An automatic target contouring system for spine SBRT is useful to reduce inter-observer differences in target definition. In this study, an automatic contouring tool was evaluated.

Methods: Simulation CT scans and MRI data of 20

patients with spinal metastases were evaluated. To evaluate the advantage of the automatic target contouring tool (Elements SmartBrush Spine), which uses the identification of different densities within the target vertebra, we evaluated the agreement of the contours of 20 spinal target (2 cervical, 9 dorsal and 9 lumbar column), outlined by three independent observers using the automatic tool compared to the contours obtained manually, and measured by DICE similarity coefficient.

Results: The agreement of GTV contours outlined by independent operators was superior with the use of the automatic contour tool compared to manually outlined contours (mean DICE coefficient 0.75 vs 0.57, p = 0.048).

Conclusions: The dedicated contouring tool allows greater precision and reduction of inter-observer differences in the delineation of the target in spine SBRT. Thus, the evaluated system could be useful in the setting of spinal SBRT to reduce contouring uncertainties, increasing the level of precision on target delineation.

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RE-TREATMENT SALVAGE FOR LOCAL RECURRENCE OF PROSTATIC CARCINOMA AFTER PRIOR IRRADIATION: AN UPDATE OF A SINGLE CENTER CLINICAL EXPERIENCE

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Aims: We evaluated the efficacy and safety of stereotactic body radiation therapy (SBRT) retreatment after an initial treatment course of radiotherapy (RT) for patients (pts) with biochemical failure and evidence of local recurrence in prostate cancer (PC).

Methods: From May 2019 to May 2022, 14 pts with evidence of clinical/radiological local relapse in the prostate or prostatic bed and no distant metastasis were retreated with SBRT. Local relapses were assessed with pelvic multiparametric MRI or PSMA/choline PET in 44% and 56% of pts, respectively. The precedent radiotherapy was delivered in 11 pts as adjuvant/salvage RT and 3 pts as radical treatment RT. At recurrence, median prostate-specific antigen (PSA) was 1.02 ng/mL (range, 0.15-1.9) in the 11 patients treated with postoperative RT and 3.5 ng/ml (range, 2.3-5.4) in patients treated radically. An androgen deprivation therapy was administered in 8 pts at the time of SBRT. The median time interval between the two treatments was five years (range 1-8). The median SBRT dose was 36 Gy (range, 25-36) in 5 consecutive fractions (range 5-6). Salvage SBRT was delivered using volumetric arc therapy (VMAT) and image-guided radiotherapy (IGRT) (Elekta Versa HD™).

Results: After a mean follow-up of 13.9 months (range, 1-24 mo), no patients had gastrointestinal and genitourinary toxicity early and/or late ≥ G3. The median age at salvage SBRT was 78 years (range, 71-86), median post-salvage SBRT PSA was 0.1 ng/mL (range, 0.0-1.1) in the adjuvant/salvage RT group and 2.75 ng ml (range, 1.8-4.2) in the radical treatment RT group. Five pts had a clinical relapse: 3 lymph nodes and two bone metastases, all outside the radiotherapy target. These patients underwent a second course of SBRT, and there is no radiological evidence of disease.

Conclusions: Our experience shows that salvage SBRT is an effective and safe treatment option, despite the small sample examined, allowing good control disease without severe toxicity.

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MANAGEMENT OF LOCAL RECURRENT PROSTATE CANCER : A SURVEY AMONG RADIATION ONCOLOGISTS OF SICILY (AIRO-SICILIA), ITALY

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Aim: To conduct a survey among Sicilian radiotherapy (RT) centers belonging to Associazione Italiana di Radioterapia ed Oncologia Clinica (AIRO), to record the different techniques, schedules, dose constraints and use of Androgen Deprivation Therapy (ADT) and to report the different toxicity profiles of re-irradiation for local recurrent prostate cancer.

Methods: Twenty-two questions concerning the re-irradiation of prostate cancer recurrence were sent on 16 May 2022 to all 19 RT centers in the region of Sicily in Southern Italy. Only one referral physician per center could answer the survey. The data requested concerned the working experience of the physician responding to the Survey, the number of retreatments performed in his center in the last year, the time interval between the first RT

treatment and re-irradiation, the RT technique adopted, the irradiated volume, the prescription dose and fractionation, the imaging techniques co-registered for treatment planning, dose constraints to organs at risk (bladder, urethra, rectum), toxicities, examinations required for re-evaluation and willingness to participate in subsequent retrospective or prospective studies on this issue.

Results: Data were collected from 6 centers.The responses showed that 83% of the colleagues surveyed had been working in radiotherapy for less than 20 years. From January to December 2021, all centers performed at least five re-irradiations in prostate cancer patients with local recurrence. 33% of the centers reported more than 20 retreatments in the last year. Regarding the timing of reirradiation, 50% of the colleagues suggested at least twelve months after the first treatment.The most frequently used technique was stereotactic body radiation therapy - SBRT (66.7%) followed by intensity-modulated RT (33.3%). RT was administered with a total dose of 35 Gy in 7 Gy per fraction in six centers (100%), 30 Gy in 6 Gy per fraction in two centers (33,3%) and 25 Gy in 5 Gy per fraction in one center (16.6%). Irradiated volume was whole prostate and simultaneous integrated boost (SIB) in recurrent site in 66.7 %, whole prostate in 16.7% and only recurrent sites in 16,6%. Dose constraints mostly used to preserve bladder were D30% < 57.9 Gy (in all centers) and 110 Gy <10cc (33,3% of the surveyed) . Rectum constraints used by all centers were D60%< 38.0 Gy, D30% < 66.0 Gy, V122.1 Gy < 5%. None used dose constraints to preserve the urethra. Grade II acute toxicity according to the Common Terminology Criteria for Adverse Events v.5 scale found was non-infectious cystitis in 33.3%. Grade 2 late haematuria was reported by two centers (33.3%) in 8% and 5% of patients respectively. No acute or late gastrointestinal toxicity was reported. All surveyed would participate in future studies.

We reported irradiated volume in Figure 1, techniques in Figure 2, delivered doses in Figure 3.

Conclusions: The present survey shows that re-irradiation of prostate carcinoma is gradually spreading in Sicily. The most widely used technique is SBRT. This is due to the progressive development of technology and medical training in Southern Italy. Although few experiences have been gathered, from the toxicities reported, re-irradiation seems to be safe.The data collected indicate a uniform approach among RT centers regarding this type of treatment. However, there was a great variability in the selection of treatment volume and a lack of information on dose constraints to the urethra.

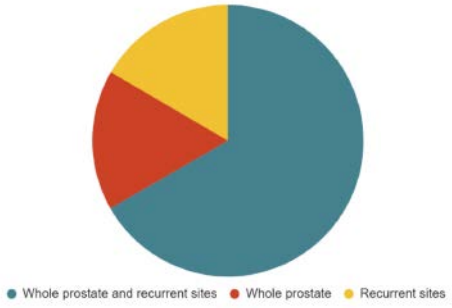

Figure 1.

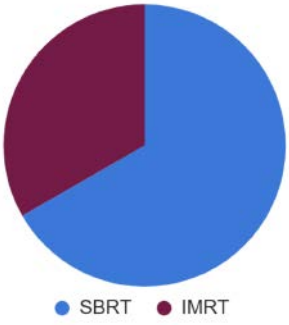

Figure 2.

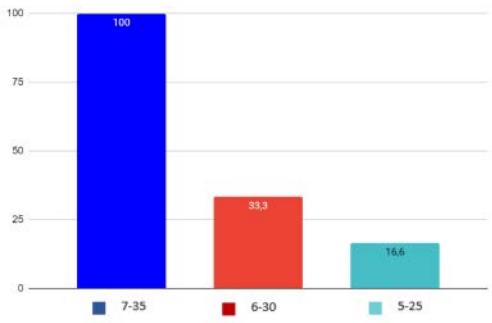

Figure 3.

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STEREOTACTIC ABLATIVE RADIOTHERAPY FOR OLIGOMETASTATIC PROSTATE CANCER

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Aims: The present study assessed clinical outcomes of stereotactic body radiotherapy (SBRT) in oligometastatic prostate cancer (PCa) patients (pts).

Methods: Between January 2017 and April 2022, we treated 52 pts for a total of 62 oligometastatic PCa sites detected with conventional and functional imaging (20 osseous and 42 nodal targets). Among these, we included, for the present analysis, 45 pts for a total of 54 lesions (18 osseous and 36 nodal targets) with a minimum follow-up of 6 months and different clinical settings: de novo oligometastatic (6 pts), oligorecurrent castration-sensitive (28 pts), castration-resistant (7 pts) prostate cancers and oligoprogressive disease during systemic therapy (4 pts). SBRT was delivered with volumetric modulated arc therapy up to a total dose of 21/24 Gy given in 3 fractions or 25/30 Gy in 5 fractions for bone lesions and 30/35 Gy in 5 fractions or 24 Gy in 4 fractions for nodal metastases. A total of 48.9% of pts (22/45) received hormonal therapy. We evaluated biochemical control [prostate serum antigen (PSA) increase < 10%], progression free-survival (PFS) (time from SBRT to biochemical and/or radiologic progression), local control (LC) (time from SBRT to in-field radiologic progression), acute and late toxicities.

Results: At 3 months, biochemical response was observed in 35/45 pts (77.8%). At a median follow-up of 21 months (range 6-63), 18/35 (51.4%) of the patients having a response at 3 months remained free from progression. Two-year PFS and LC were 46% and 88%, respectively. In-field progression occurred in 7/54 (13%) lesions. Hormone/systemic therapy was delayed by an average of 13.6 months (range 3-44). No significant difference in PFS based on the type of lesion or concomitant endocrine therapy was observed and no toxicity grade > 2 was reported.

Conclusions: SBRT for oligometastatic prostate cancer patients offers a good rate of biochemical/local control and tangible delay in hormone/systemic therapy without major toxicities.

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BREAST CANCER AND OLIGOMETASTATIC BONE DISEASE (OMBD): EVALUATION OF LOCAL CONTROL AND TIME TO PROGRESSION IN PATIENTS TREATED WITH ABLATIVE RADIOTHERAPY (ABRT)

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Aims: To evaluate local control, local relapse, and acute toxicity in patients treated with ABRT for oligometastatic breast cancer bone disease (OMBD).

Methods: From January 2017 and January 2022 we retrospectively evaluated all oligometastatic bone patients and among these we selected who had primary breast cancer diagnosis treated to our center. All patients had a life expectancy major of 6 months, Karnofsky Performance Status > 60 and number of lesions 1 > 5, histological diagnosis of invasive breast cancer, clinical and imaging confirmed diagnosis of oligometastatic disease.

Results: In the period of observation, 65 OMBD patients were treated with ablative Radiation Therapy using different schedules of fractionation. Ten patients were lost during follow-up. 55 patients and 118 lesion were evaluated; 23.6% showed synchronous primitive and secondary disease and 76.4% were metachronous. Median age was 58 (range 30 – 86 years) at the time of the first radiation treatment. All patients were submitted to different combined or alone schemes of endocrine-chemo-biotherapy. Regarding techniques, 36,4% SBRT, 40,2% IMRT and 23,4% 3DCRT have been used respectively. Among these 27.3% of the treatments were delivered using a single fraction and in 72.7% a fractionation course has been choosen. The median total dose delivered was 19.5Gy (range 12-27Gy) in 1-3 fx. The median follow-up was 26 months (6-60 months), 14.6% of the patients needed a retreatment for local relapse (LR) and 85.4% showed local control at 24 months after the treatment. Toxicities have been evaluated according to CTCAE v4: radiodermatitis G1 in 51% have been registered, and radiodermatitis with pain G2 occurred in 11% of the patients. No higher toxicities >G3 have been recorded.

Conclusion: In our experiences treating OMBD, ABRT has shown to be efficacy, well tolerated with low grade toxicities, and with promising local control rates.

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PROSTATE CANCER: HYBRID IMAGING WITH PET/CT GUIDING SALVAGE PROSTATE RE-IRRADIATION OR MULTI-SITE METASTASIS IRRADIATION WITH STEREOTACTIC BODY RADIOTHERAPY

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Aims: We retrospectively evaluated the feasibility and the toxicity of a prostate re-irradiation after definitive/salvage radiation therapy failure and multi-site prostate recurrences with SBRT using functional imaging with PET/CT as a target guide for stereotactic body radiotherapy (SBRT) .

Methods: Between January 2019 and June 2021 eight men (mean age 63 years, 44-84) in androgen deprivation therapy had imaged proven recurrences of prostate cancer after definitive prostate radiation therapy. Four cases with intra-prostatic relapses (group 1) and four patients with bone and lymphatic recurrences (group 2) underwent respectively to a salvage SBRT of the prostatic lodge with a total dose of 35 Gy delivered in 5 fractions over 5 consecutive days (group A) and to a personalized total dose in 2 to 5 consecutive fractions (group B), ranging from 700 to 1000 cGy per fraction. PSA variation levels were considered as a biological response in all cases. Prostate MRI, 18F-Cholina or PSMA PET/CT were performed in all patients according to the PSA level at the time of the biological relapse. All patients in group B underwent a re-staging with PET/CT. Post-radiation complications were recorded using the Common Terminology Criteria for Adverse Events (CTAE v 4.03) and compared to the baseline status

Results: In group A, a biochemical positive response was recorded in all patients and none of them, within a median follow-up period of 12 months, had local recurrences. In group B, PSA regression levels were present in three patients, one man experienced biochemical progression despite a complete response to SBRT in all treated sites. This patient had three radiation sections with SBRT in multiple focal bone lesions (most of them with 1000cGy in each fraction), his PSA levels two months after the last SBRT reached 15.5 ng/mL, PSMA PET/CT showed total response in the treated bone lesions which became dense at CT without enhancing tracer, despite the onset of new distant bone involvements. The observed toxicity at the end of the follow up was < 2 grade in all patients. No CTAE grade 3-4 was registered.

Conclusion: Functional imaging applied as target volume of SBRT in local or distant recurrences from prostate cancer in case of re-irradiation and /or multi-oligometastatic sites is an effective and feasible option to offer to patient in order to improve their outcome. Long-term data and larger cohort of patients are compulsory.

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STEREOTACTIC RADIOTHERAPY FOR TREATMENT OF BRAIN METASTASES: A MONOCENTRIC EXPERIENCE

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Aims: Brain metastases (BM) are a common complication in a variety of malignancies, but they're particular frequent in lung cancer patients. Stereotactic radiation (SRT) has become a popular non-invasive therapeutic option for patients with BM in recent decades. In this retrospective study, we want to evaluate the role of SRS in patients with non-small-cell lung cancer (NSCLC) BM

Method: Between July 2011 and October 2021, a total of 121 pts (median age 67, M: F 1,5: 1) presenting with 187 metastases were submitted to SRS with brain metastases were submitted to SRS. The RT treatment was performed with True Beam LINAC VARIAN System with IMRT technique, using 6MV photons. We utilized a head thermoplastic mask as immobilization system. All of them had Karnofsky PS ≥70. Planning tumor volume was obtained by adding to GTV an isotropic margin of 3 mm in all directions. Radiological response on MRI was assessed by a neuroradiologist according to the RANO-BM criteria. Local control was defined as the absence of new radiographic enhancing abnormality in the irradiated areas on MR imaging. Brain progression-free survival (BPFS) and Overall Survival (OS) rates from the diagnosis of BM were calculated from the date of first radiotherapy treatment using the Kaplan-Meier method. In this analysis we evaluated results in terms of local control, overall survival and radiation induced brain necrosis, trying to find a correlation with the the delivered dose and the planning volume.

Results: After a mean follow-up of 19 months, 83 metastases (44,3%) were in progression. In all patients local control and lower metastases volume were found to be predictive of increased OS ($p = 0.001$ and $p = 0.004$ respectively). High BED 10 and BED 12 values correlated with a better prognostic outcome ($p < 0.001$ and $p < 0.001$). 71 patients (58.6%) showed a radionecrosis at MRI performed during follow-up. This reaction wasn't statistically related to GTV-volume or delivered dose.

Conclusions: Local control and OS appears to be dose and volume dependent.

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TREATING NODAL METASTASIS WITH PALLIATIVE INTENT: STEREOTACTIC BODY RADIOTHERAPY (SBRT) TO POSITIVE CHOLINE PET / CT LYMPH NODES FOR OLIGOMETASTASIZED PROSTATE CANCER (PCA) PATIENTS

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Aims: The purpose of this study is to evaluate the feasibility and toxicity of based stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer (PCa) patients.

Methods: In this study, oligometastasized PCa patients with nodal (≤ 3 lesions) were treated using SBRT in association with androgen-deprivation therapy. All patients were studied with Choline PET/CT before RT. The prescribed SBRT to pathologic lymph nodes was 8 Gray (Gy), delivered in three fraction to have a better control of organ motion (bowel above all) and normalized so that the 80% isodose covers 100% of the PTV.

Results: Between January 2019 and December 2021, 119 oligometastasized PCa patients with nodal metastasis were treated stereotactic on positive choline PET / CT lymph nodes. At a median follow-up of 4 (1-10) months, no toxicity was observed and a reduction in the volume of irradiated lymph nodes in 60% of patients. Only 5%of the disease progressed, while the remaining lymph node volume was stationary. All patients were re- evaluated with PET/CT.

Conclusions: SBRT to positive choline PET / CT lymph nodes for oligometastic prostate cancer is a feasible treatment modality with minimal toxicity. Further studies with a longer follow-up are needed to better evaluate late toxicity and local control.

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HYPOFRACTIONATION IN THE TREATMENT OF BONE METASTASES IN PATIENTS WITH HORMONE REFRACTORY PROSTATE CANCER

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Aims: The hypofractionated radiotherapy plays a fundamental role in the treatment of bone metastases. At our center, we evaluated the feasibility and effectiveness of two schemes hypofractionation: 8 Gy single dose and 8 Gy in two fractions to be made within a week of each other. The two irradiation techniques have been associated with the new molecules used in medical therapy.

Methods: From July 2014 to March 2022 they were treated 160 patients with bone metastases from hormone refractory prostate cancer . The median age of patients studied was 71 years with bone metastasis respectively localized in the dorsal and lumbar spine in 50% of cases, 30% at the level of bilateral lower limbs and the remaining 20% at the level of the pelvis. Radiation therapy was by hand in a single dose in 60% of cases in patients with worse P.S. while in the remaining 40% it was backed bifractionation treatment.

Results: All patients were reassessed after 30-40 days of therapy. In no case were registered signs of toxicity. In 80% of cases there has been a reduction in their analgesic therapy administered dose.

Conclusions: In our experience, the radiotherapy hypofractionated 8 Gy in a single session or, alternatively, 8 Gy in two weekly sessions was well tolerated and had a good impact both as regards the control of the pain is the improvement of quality of life.

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A RARE CASE OF ROSAI-DORFMAN SYNDROME WITH ISOLATED CENTRAL NERVOUS SYSTEM INVOLVEMENT RE-TREATED WITH HYPERARC TECHNIQUE

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Aims: Rosai-Dorfman disease (RDD) is a rare benign lymphoproliferative disorder characterized by infiltration of tissues by non-malignant histiocytes and can involve any nodal or extranodal site. Central nervous system (CNS-RDD) involvement is infrequent accounting for only 4% of all reported cases. Intraparenchymal involvement is uncommon. Due to the rarity of CNS involvement, there are no uniform treatment recommendations. When feasible, surgical resection is usually the therapy of choice but, when it is not possible, other therapeutic modalities may be considered. A case of a man with isolated CNS-RDD treated with repeated cycles of Radiotherapy is here reported to show the good disease control that Radiotherapy can obtain in this setting of patients.

Methods: In 2017, a 51-year-old man was diagnosed with CNS-RDD presenting with three enhancing intraparenchimal lesions in the right peritrigonal, left paratrigonal and left occipital regions and perilesional edema. Declared inoperable, in 2018 he was subjected to stereotactic radiotherapy on the three sites of brain disease to a

dose of 37.5 Gy in 5 fractions, obtaining a partial response. He came to our center in 2021 following worsening of symptoms (balance and speech disturbances, intense headache, visual disturbances, lower limb strength deficit) not responsive to cortisone therapy and radiological evidence of new disease progression. He was then subjected in July 2021 to a re-irradiation of the three brain locations. In order to minimize the dose to healthy brain tissue, it was used the HyperArc (Varian) VMAT planning approach using 4 photon non-coplanar arcs 6 MV to a dose of 20 Gy in 10 fractions of 2 Gy.

Results: The treatment was well tolerated and the patient presented a rapid resolution of the symptoms already at the first follow-up (disappearance of speech and vision disorders and headache, marked improvement in balance and weakness of the lower limbs) with a radiologically responsive disease and resolution of cerebral edema around the lesions. At 1 year follow-up, the patients shows further improvement in symptoms with radiologically stable disease.

Conclusions: Radiotherapy is a feasible, well tolerated and effective approach in the treatment of CNS-RDD. Highly conformed techniques such as VMAT with HyperArc planning approach can be used for reirradiation in patients presenting with disease relapse with excellent tolerance and response to treatment.

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STEREOTACTIC RADIOTHERAPY'S EFFICACY IN PATIENTS WITH LUNG OLIGOPROGRESSIVE METASTATIC ADENOID CYSTIC CARCINOMA

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Aims: This case illustrates disease control by stereotactic radiotherapy of a patient who was diagnosed with left parotid carcinoma in 2013, relapsed in 2014, and has been in lung metastatic progression since 2016.

Materials and Methods: A 79-year-old man was diagnosed with left parotid cancer in 2013 and subsequently had surgery. Histological analysis revealed adenocystic carcinoma with facial nerve infiltration (T4aN0M0) hormone receptor expression negative , which was treated with 63 Gy on the parotid loggia and 54 Gy on the left laterocervical lymph nodes. in July 2014 a disease recurrence in the left cavernous sinus was treated successfully with Cyberknife at a total dose of 21 Gy in three fractions. He has been doing radiological follow-up exclusively since 2017. In September 2017 CT(computer tomography) scan showed the appearance of a right lower lobe and a left lower lobe and parascissural lesions treated with stereotaxis radiotherapy with the radiation dose respectively of 24 Gy in one fraction and 30 Gy in 3 fractions. In 2018 3 new nodule appeared on chest CT scan during follow up , so a new radioterapic treatment was performed stereotactic therapy on three lung lesions on 2 on right upper lobe and a upper lower with the radiation dose respectively of Gy in one fraction and 30 Gy in 2 fractions. He has been doing radiological follow-up exclusively since 2018. Disease to remain stable until February 2022, as new pulmonary middle and the left parailar nodules emerged and both treated with radiosurgery (24 Gy in single fraction). The patient never received any kind of systemic therapy.

Results: The patient received multiple stereotactic radiotherapy treatments from 2014 and 2022, with a good response and regression of the lesions described. Patient is in good overall health, eupnoic, and has no respiratory symptoms at this time.

Conclusions: In selected patients (oligoprogressive disease), stereotactic radiotherapy can be a safe and effective weapon for local disease control. SBRT is an excellent weapon in the treatment of patients with oligoprogressive adenoid cystic carcinoma.

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SELECTING PATIENTS FOR SRT IN OLIGOMETASTATIC SPECTRUM: A PRACTICAL GUIDE

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Aims: Before 1995, cancer history was divided in 2 big category: locally confined disease and metastatic status. Hellman and Weichselbaum introduced oligometastatic disease (OMD) defined by a transitional state before systemically metastasized disease where it is possible to stop or to slow down cancer widely dissemination. In fact, a local approach such as Stereotactic Radiotherapy (SRT) combined with primary systemic therapy could guarantee local control improving patients' outcomes and progression free survival (PFS) as several phase 2 trials are confirming. It is crucial to select patients in OMD to obtain potential ablative results by combined therapies. The aim of this work is to report the OMD spectrum in a pocket guide for daily clinical practice.

Methods: PubMed was explored for clinical trials, reviews, retrospective analysis on OMD. In particular, EORTC-ESTRO and ESTRO-ASTRO consensus documents were considered.

Results: Both consensus identify 3 areas for OMD: *De Novo, Repeat and Induced OMD*, defined as first-time oligometastases diagnosis, previous history of OMD and conversion of polymestastic diseases in OMD, respectively. Depending on time of diagnosis, they agreed on terminology but not on range in months: for EORTC/ESTRO, *synchronous* is OMD diagnosis in <6

months since primary cancer diagnosis (vs. simoultanealy for ESTRO/ASTRO) and *metachronous* >6 months (vs. 3-6 months for ESTRO/ASTRO). EORTC/ESTRO Consensus got deeper in the OMD characterization with more sub-classification: *Oligorecurrence* occurs when therapy succeed in controlling metastasis but a new OMD diagnosis is detected in the treatment-free interval; instead, *Oligoprogression* and *Oligopersistence* scenarios, during active systemic therapies. The first one is described by the growth of new or known metastasis, the second one by the stability of OMD. Both terms symbolize a partial or no response to treatments. All the examined trials identify the combination of local and systemic treatments as the best OMD therapy strategy. The key point is that an appropriate OMD classification results in a documented favorable impact on PFS compared to systemic therapy alone (Table 1).

Conclusions: Consensus delineate different settings in the oligometastatic spectrum. Appropriate OMD classification reported in a practical guide for daily clinical use allows both to select patients and to offer the best therapeutic approach in this disease setting mostly for the possible ablative results.

Table 1. Definitions of OMD and PFS in the considered trials according to OMD classification.

ESTRO/EORTC CONSENSUS		ESTRO/ASTRO CONSENSUS		Authors	Primary Tumor	Therapy	PFS (Months)
De novo oligometastatic disease (First time oligometastases diagnosis)	**Synchronous/Metachronous oligometastatic disease:** • +/− 6 months from primary cancer diagnosis, respectively	**Synchronous/Metachronous oligometastatic de novo disease:** • Limited number of metastases found simultaneously with primary tumor or by 3-6 months after its diagnosis	Gomez et al. 2016	NSCLC	Local + Systemic Therapies	25 vs 11 (Only Maintenance)
			Iyengar et al. 2018	NSCLC	SBRT + Systemic Therapies	40 vs 11 (Only Maintenance)
			Ahmed et al. 2019	NSCLC	SBRT + Systemic Therapies	19
			Harrow et al. 2019	Prostate	Local + Systemic Therapies	19 vs 12 (Only ADT)
			Parker et al. 2018	Prostate	SBRT + Systemic Therapies	36 vs 21 (Only ADT)
	Metachronous oligorecurrence: • No active systemic therapy • Diagnosis of new metastases > 6 months from primary cancer diagnosis	**Metachronous oligometastatic disease or Oligorecurrence disease:** • Diagnosis of new metastases > 6 months from primary cancer diagnosis • All states of repeat OMD	Ost et al. 2017	Prostate	SBRT + Systemic Therapies	28 vs 11 (Only Surveillance)
			Triviai et al. 2018	Prostate	SBRT + Systemic Therapies	24
			Berchtold et al. 2018	Prostate	SBRT + Systemic Therapies	27
	Metachronous oligoprogression: • No active systemic therapy • Diagnosis of new metastases > 6 months from primary cancer diagnosis					
	Repeat oligometastatic disease: • No active systemic therapy • Diagnosis of new metastases					
Synchronous oligometastatic disease (after local or systemic or both therapies, new diagnosis of oligometastases)	**Repeat oligorecurrence:** • Active systemic therapy • Diagnosis of new or growing metastases		Hasselmann et al. 2012	NSCLC	Local + Systemic Therapies	10
			Iyengar et al. 2018	NSCLC	SBRT + Systemic Therapies	40
			Ahmed et al. 2019	NSCLC	SBRT + Systemic Therapies	19
			Ost et al. 2017	NSCLC	Local + Systemic Therapies	7
	Repeat oligoprogression: • Active systemic therapy • Presence of new oligometastatic metastases		Lievens et al. 2014	Prostate	SBRT + Systemic Therapies	40% at 24 months
			Ahmed et al. 2019	Prostate	Local + Systemic Therapies	19
Induced oligometastatic disease (history of oligometastatic disease)	**Induced oligorecurrence:** • No active systemic therapies • Diagnosis of new metastases	**Induced oligometastatic disease:** • Development of OMD after systemic therapy in polymetastatic patients				
	Induced oligoprogression: • Active systemic therapy • Diagnosis of new or growing metastases					
	Induced oligometastases: • Active systemic therapy • Presence of new oligometastatic metastases					

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PHOTON-BASED HIGH-DOSE SINGLE-FRACTION RADIOSURGERY, AN EFFECTIVE TREATMENT MODALITY FOR RECURRENT UVEAL MELANOMA: A CASE REPORT

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Aims: To evaluate and report the outcome of a patient with locally recurrent uveal melanoma previously treated with brachytherapy using a second personalized globe-sparing radiotherapy approach.

Methods: In June 2020, a 78 years old man arrived at our Institution with diplopia and suspected uveal melanoma (UM). At the ophthalmological evaluation (B-scan, A-scan and UBM) a lesion in the right eye at 6-7 hours of about 5 mm thichness, with internal lacunar areas, approximately 7 mm away from the limbus, was observed. The patient underwent ruthenium plaque brachytherapy (BT) at a total dose of 110 Gy at the apex of the tumor. At the follow-up, the lesion was under control until September 2021, but recurred with a satellite exudative detachment in the lower and temporal sectors from 7 to 10 hours. At the B-scan the lesion had a maximum thickness of 4.6 mm. Subsequently in a multidisciplinary discussion and in consideration of the non-feasibility of a new positioning of plaque, one single fraction radiosurgery (SRS) was scheduled. A CT simulation was performed using an immobilization thermoplastic mask and an eye fixation system. Dosimetric data from both the primary treatment and the re-irradiation were merged, making it possible to determine the overdosage volume. So, the prescribed dose was 27 Gy in the de-novo lesion and 24 Gy in the previously irradiated volume in order to respect the tolerance of structures at risk. SRS was performed on 21 October 2021.

Results: The time interval between the two treatments was 15 months. After a follow up of 8 months the local tumor control was satisfactory and no metastases were detected on follow-up examinations. Furthermore, there was a reabsorption of the initial exudative detachment. No severe acute or late toxicity was observed due to the retreatment. The only late adverse event was cataract grade 2 (CTCAE vs. 5.0).

Conclusion: Photon SRS is a feasible, acceptably tolerated modality and represents an eye-preserving treatment also for patients with recurrent UM unfit for BT.

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PROPHYLACTIC RADIOTHERAPY OF HETEROTOPIC OSSIFICATION: AN AMSTAR-COMPLIANT SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS AND META-ANALYZES

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Aims: Heterotopic ossification (HO) is a frequent complication after total hip arthroplasty. Several prophylactic treatments for hip HO have been proposed and radiotherapy (RT) has been used in this setting. The aim of this review is to provide an overview of the evidence of systematic reviews and meta-analysis on RT efficacy in preventing hip HO.

Method: A literature search was conducted on PubMed on 30 May 2021 as follows: "heterotopic ossification" AND "hip" AND ("radiotherapy" OR "radiation"). We included in this paper all systematic reviews and meta-analyses published in English after 1990. The quality of the analysis included in this review was independently performed, using the AMSTAR-2 tool (A MeaSurement Tool to Assess systematic Reviews) by two different authors. The overall confidence rating, based on AMSTAR-2 guidelines, was defined as follows: i) "high", in case of 0-1 non-critical flaw, ii) "moderate", in case of >1 non critical weaknesses; ii) "low", in case of 1 critical weaknesses +/- critical flaws; iv) "critical low", in case of >1 critical weaknesses +/- non-critical flaws.

Table 1. Characteristics and results of the included systematic reviews and meta-analyses.

Authors, year	Review type	No. and design of studies	No. of patients	Setting	Comparisons	Main findings
Pakos et al., 2004	MA	8: 7 RCTs 1 Non-RCTs	1143	HOP	RT vs NSAIDs	• No difference between the two arms considering all HO grades (RR: 0.75, 95% CI, 0.37-1.71) • RT more effective than NSAIDs in preventing Grade III-IV HOs (RR: 0.42; 95%CI, 0.18-0.9, p:0.043).
					Preop RT vs Postop RT	• Random effects RR after preop RT: 4.30 (1.91-9.70): after postop RT > 8 Gy: 0.17 (0.08-0.36).
					RT dose	• Significant dose-response relationship in patients treated with postop RT (p: 0.008).
Vavken et al., 2009	SR & MA	9: 8 RCTs 1 Non-RCTs	1295	HOP	RT vs NSAIDs	• No statistically significant difference among RT and NSAIDs (p: 0.474). • No difference in risk of complications between the two arms (p: 0.431).
Popovic et al., 2014	SR & MA	61: 14 RCTs 34 Non- RCTs 12 NR	5464 sites	HOP/HORP	Preop RT vs postop RT	• No significant differences between postop and preop RT in terms of B III-IV HTO (p: 0.1). • Postop treated sites developed B I-II HO more than those treated preoperatively (p: 0.05).
					RT dose	• After adjusting for RT site, no significant impact of prescribed RT dose (p: 0.1).
Milakovic et al., 2015	SR & MA	12 RCTs	1253 sites	HOP/HORP	Preop vs postop RT	• Overall prevalence of HO: postop RT: 32.4%, preop RT: 42.2% (p: 0.43). • B I-II HO were 35.8% and 29% in the preop and postop RT groups, respectively (p > 0.05).
					BED > 25 Gy vs ≤25 Gy	• BED ≤ 25 Gy: 26.4% HO (B I-II HO: 23.5%). BED > 25 Gy: 42.8% HO (B I-II: 37.7%).
				HORP	Preop vs postop RT	• No difference in HO progression between preop vs postop RT (p : 0.43)
					BED > 25 Gy vs ≤25 Gy	• No difference in HO progression between high and low BED (p : 0.28).
					SFRT vs MFRT	• MFRT more effective than SFRT in reducing HO risk (p:0.04); B: I-II (p:0.0009), III-IV HO (p : 0.32).
Cai et al., 2019	MA	31 RCTs	7769	HOP	Nonselective and selective NSAIDs vs RT vs controls	• Lower HO rate after nonselective NSAIDs, selective NSAIDs and RT vs control (OR=0.34, 95%CI 0.22-0.51; OR=0.42, 95%CI, 0.24-0.73; OR=0.17, 95%CI 0.076-0.37, respectively). • Lower HO rate after nonselective NSAIDs, selective NSAIDs vs RT: (OR=0.50, 95%CI 0.25-1.0; OR=0.41, 95%CI, 0.17-0.97, respectively). • Lower incidence of postop toxicity after selective NSAIDs vs nonselective NSAIDs, controls and RT.
Hu et al, 2021	SR & MA	10 RCTs	1203	HOP/HORP	Preop RT vs postop RT	• Preop RT: HO=25.2% (21.6 % B I/II and 3.7% B III/IV); postop RT: HO=18% (16% B I/II and 2% B III/IV) (p: NS) • HO - 5/1 Gy: postop RT: 30.1%, preop RT: 14%; 7/1 Gy: postop RT: 17.5%, preop RT: 29.3%; 8/1 Gy: postop RT: 23.9%, preop RT: 24.5%. (p: NR)
					SFRT vs MFRT	• SFRT: HO=25.6% (22.9% B I/II and 2.7% B III/IV); MFRT: HO=12.1% (10.3% B I/II and 1.8% B III/IV) (p : NR)
				HORP	Preop RT vs postop RT	• No difference between preop and postop RT for overall progression of HO (p : 0.43).
					Low BED group vs medium BED low vs high BED group medium vs high BED group	• Lower HO progression in medium vs low BED (p: 0.003). (B I/II HO. P < 0.0001; B III/IV HO, p : 0.73) • No difference in low vs high BED group (p:0.21). • NR
					SFRT vs MFRT	• Higher overall HO progression after SFRT vs MFRT (p : 0.04), especially for B I/II HO (p : 0.003) compared to B III/IV HO (p : 0.55).
Shapira et al., 2021	SR & MA	37: 27 RCTs 10 Non-RCTs	8653	HOP	RT vs NSAIDs vs no treatment	• Patients without HO: RT: 28.6 %-97.4% (severe HO: 0.0%-11.9%); NSAIDs: 76.6%-88.9% (severe HO: 0.0%-1.8%). NSAIDs may be more effective than RT in high-risk patients.

Legend: B: Brooker; BED: Biologically Effective Dose; HO: heterotopic ossification; HOP: heterotopic ossification prophylaxis; HORP: heterotopic ossification recurrence prophylaxis; MA: meta-analysis; MFRT: multifractionated radiotherapy; NR: not reported; NS: not significant; NSAIDS: nonsteroidal anti-inflammatory drug; postop: postoperative; preop: preoperative; RCT: randomized controlled trial; RR: risk ratio; THA: total hip arthroplasty; RT: radiotherapy; SFRT: single fraction radiotherapy; SR: systematic review.

Results: Seven systematic reviews and meta-analysis were included. Characteristics and results of the included articles are summarized in Table 1. In three studies the prophylactic setting of recurrence was also considered. The efficacy of RT and anti-inflammatories seems to be equivalent, with an RT advantage reported in one study in preventing grade III and IV HO (RR: 0.42; 95%CI, 0.18-0.9, p: 0.043). Not significant difference between postoperative and preoperative RT in both primary and secondary prophylaxis, with a slightly higher incidence of HO when RT is delivered before surgery, was reported by two reviews. In one meta-analysis, a significant dose-response relationship was observed in patients treated with postoperative RT (p: 0.008). No difference in HO progression between high and low BED were found in two reviews (p: 0.28; p: 0.21). Based on the assessment of the quality of the studies, one and two analyses were classified as moderate and low overall confidence rate, respectively. The AMSTAR 2 domain with the highest number of critical weaknesses was "Impact of risk of bias on pooled results".

Conclusions: Although RT is a well-established prophylactic treatment for hip HO, the optimal RT setting and dose still remain undefined. Further studies should be designed to clarify the role of RT as an alternative to the use of anti-inflammatory drugs in this setting.

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IS IT POSSIBLE TO INCREASE THE USE OF PALLIATIVE RADIOTHERAPY IN PATIENTS WITH BONE METASTASES? RESULTS OF A SINGLE-CENTER OBSERVATIONAL STUDY

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Aims: Radiotherapy (RT) is an effective palliative treatment in patients with bone metastases. However, many studies and clinical practice highlight a number of barriers hindering the use of RT: difficulty in traveling to reach a RT center for patients with advanced cancer, concern about the need for prolonged therapies, delay in consultations and in the treatment or complicated referral process or difficulty in contacting the radiation oncologists (ROs), difficulty in predicting prognosis in cancer patients, consequent risk of RT delivery near the end of life, and poor knowledge of RT by specialists in palliative care. Since 2015 in our center we have tried to remove some of these barriers to favor the use of palliative RT in this setting. The purpose of this report is to describe the methods and results of this experience.

Methods: This is a single-center observational study on patients undergoing RT for bone metastases (1065/2020/Oss/AOUBo). Starting from 2015, the following measures were adopted: i) simplification of RT referral and planning; ii) introduction of abbreviated treatments (single fraction, sterotactic RT, accelerated-hypofractionated RT with daily bifractionation; iii) assigning palliative treatments to a single ultra-specialized RO; iv) participation of the latter in a MDT for bone metastases. Data were collected on patient characteristics (age, gender, home site, use of systemic therapies), prescribing physicians, bone metastases, and RT dose and

fractionations. Statistical analyses were performed with the SPSS package and R software.

Results: During the reporting period, 1283 RT treatments were performed in 900 patients with bone metastases (Table 1). The analysis showed a significant and progressive increase in RT treatments of bone metastases from 129 cases in 2014 to 234 cases in 2021 (p<0.001). This increase was observed for all anatomical sites, for both complicated and non-complicated metastases, and particularly involved the shortest treatments. The most widely used regimen was based on 8 Gy single fraction which was the treatment with the greatest increase over the reporting period. Finally, a significantly increased use of palliative RT was recorded within all analyzed subcategories.

Conclusions: Our analysis showed that simplifying procedures, accelerating planning and delivery, dedicating an RO to palliative RT, and intensifying interdisciplinary collaboration leads to significantly greater use of palliative RT in bone metastases.

Table 1. Time course of radiotherapy treatments in patients with bone metastases.

		2014		2015		2016		2017		2018		2019		2020		2021		p
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Treatment site	Spine	633	49.3	64	49.6	53	47.7	49	51.0	76	52.1	91	47.4	86	53.8	100	46.5	114	48.7	
	Extremities	183	14.2	21	16.3	27	24.3	20	20.8	19	13.0	21	11.0	16	10.0	22	10.3	37	15.8	
	Pelvis	299	23.3	34	26.4	27	24.3	18	18.8	31	21.2	45	23.4	30	18.8	57	26.5	57	24.4	< 0.001
	Skull	19	1.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	13	6.0	5	2.1	
	Rib	37	2.9	2	1.6	0	0.0	3	3.1	3	2.1	4	2.1	1	0.6	9	4.2	15	6.4	
	Others	112	8.7	8	6.2	4	3.6	6	6.2	17	11.6	30	15.6	27	16.9	14	6.5	6	2.6	
Treatment site	Spine	633	49.3	64	49.6	53	47.7	49	51.0	76	52.1	91	47.4	86	74	100	46.5	114	48.7	
	Non- Spine	650	50.7	65	50.4	58	52.3	47	49.0	70	47.9	101	52.6	53.8	46.2	115	53.5	120	51.3	0.893
Metastatic type	Complicated	848	66.1	99	76.7	89	80.2	71	74.0	112	76.7	150	78.1	129	80.6	106	49.3	92	39.3	
	Non-complicated	435	33.9	30	23.3	22	19.8	25	26.0	34	23.3	42	21.9	31	19.4	109	50.7	142	60.7	< 0.001
RT fractionation	8x1	436	34.0	7	1.6	56	12.8	32	7.3	56	12.8	60	13.8	88	20.2	65	14.9	72	16.6	
	20x5	418	32.6	49	11.7	51	12.2	51	12.2	57	13.6	64	15.3	39	9.3	50	11.9	58	13.8	
	30x10	148	11.5	71	48.0	2	1.4	9	6.1	6	4.1	20	13.5	11	7.4	17	11.5	12	8.1	< 0.001
	Stereotactic	49	3.8	0	0.0	0	0.0	2	4.1	1	2.0	7	14.3	0	0.0	17	34.7	22	44.9	
	Accelerated bifractions	82	6.4	0	0.0	0	0.0	0	0.0	2	2.4	9	10.8	2	2.4	36	43.4	34	41.0	
	Others	150	11.7	2	1.4	2	1.4	2	1.4	24	16.2	32	21.6	20	13.5	30	20.0	36	24.3	
Total treatments		1283	100.0	129	10.0	111	8.6	96	7.5	146	11.4	192	15.0	160	12.5	215	16.8	234	18.2	< 0.001

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INCREASING RELUCTANCE TO ADJUST PAIN DRUG THERAPY AS THE CLASS OF ANALGESICS GROWS. A MULTICENTER ANALYSIS ON 2104 PATIENTS FROM 13 RADIOTHERAPY DEPARTMENTS

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Aim: Pain is one of the most common symptom among cancer patients, occurring in 30-50% of patients undergoing active antineoplastic therapy and in 75-90% of patients with advanced stage tumor. Furthermore, studies on pain assessment during radiotherapy (RT) are lacking. The aim of this multicenter observational prospective trial was to evaluate the prevalence of pain in RT departments using the Numeric Rating Score (NRS). Moreover, we analyzed the correlation between pain intensity and classes of used analgesic drugs.

Methods: In this study we enrolled 2104 patients from 13 RT Departments. RT aims and patients and pain characteristics were recorded, using a collection form, during patients visits (in the course or at the end of treatment). The Pain Score was graded from 0 (no pain; NRS: 0) to 3 (severe pain; NRS: 7-10). An Analgesic Score was defined with values between 0 (no pain medication) and 3 (use of strong opioids). This study was approved by the Ethical Committee of the participating centers (ARISE-1 study).

Results: Of enrolled patients, 67.3% had pain or were under analgesic treatment. Among them, 53.8% complained of intermediate to severe pain. The incidence of intermediate/severe pain was found to increase progressively from patients not taking analgesic drugs, to those taking non-opioid drugs, to those taking weak opioid drugs, showing a clearly lower willingness to prescribe drugs of a higher class as the same increased (30%, 46%, and 83%, respectively; p<0.001; Figure 1). Moreover, patients under strong opioids reported moderate/severe pain in 75% of cases.

Conclusions: This analysis shows persistent barriers to the use of strong opioid even in cancer patients. Furthermore, our study shows the frequent ineffectiveness of opioid therapy in this setting, probably, at least in

part, due to suboptimal doses or posology. Therefore, further efforts are needed to improve pain management, particularly in the RT settings. In particular, both training in pain therapy for radiation oncologists and closer multidisciplinary collaboration are needed for this purpose.

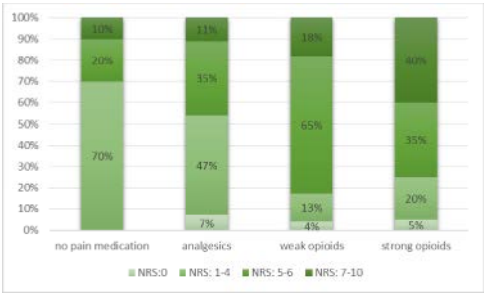

Figure 1.

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USE OF A NEW BIPHASIC MATRIX (KOLLIPHOR P407) GEL FORMULATION IN THE PREVENTION AND TREATMENT OF RADIODERMATITIS: A MONO INSTITUTIONAL PILOT STUDY

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Aims: Assess the efficacy and tolerability of a new biphasic matrix (Kolliphor P407) gel formulation in prevention and treatment of radiodermatitis in patient with breast cancer treated with hypofractionated radiotherapy. This medical device contains Hyaluronic Acid, Calendula Officinalis, Aloe Vera and EGCG (Epigallocatechin-gallate). All of these products have well-known antinflammatory, moisturizing and healing properties. Moreover, the biphasic matrix ensures the creation of a protective film on the skin with an optimal barrier effect, a good heat dispersion and the delivery of hyaluronic acid beyond epidermidis.

Methods: Patients used the medical device throughout the duration of radiotherapy and for two weeks afterwards. Using CTCAE skin toxicity grading scale, patients were monitored before therapy, weekly during therapy, and for ten days after radiotherapy was completed. Patients received a 3D conformal hypofractionated radiotherapy schedule (50-57.5 Gy with SIB technique on breast and tumor bed) in daily fractions of 2-2.3 Gy with 6-15 MV photons. All the enrolled patients were given a self-made five items questionnaire to evaluate cosmetic tolerability of the cream. The maximum toxicity data during treatment has been compared to an historical cohorts with standard of care.

Results: Between December 2021 e March 2022, 47 consecutive patients were enrolled in this study. Median age of the patients was 58 (range 29-85). No patient had previous skin conditions before RT. Grade I – CTCAE dermatitis was assessed in 9 patients (19%) during the second week of RT, in 23 patients (48%) during the third week, and in 5 patients (11%) during the fourth week. The maximum radiation induced skin toxicity observed during the treatment was: Grade I toxicity, 58% (27 patients); grade II toxicity, 38% (18 patients); grade III toxicity, 4% (2 patients). No acute gel related side effect were observed. All patient ended RT scheduled treatment. Ten days after RT, only 8 patient had residual skin toxicity. These data were consistent with those of the historical cohort. The questionnaire administered showed an average score of 11 points out of 15 available, with optimal tolerability.

Discussion: This new biphasic matrix (Kolliphor P407) gel formulation is a safe and acceptable formulation to acute prevention and treatment of breast cancer's patients skin toxicity profile. In these patients, the toxicity data were similar to our stardard of care with optimal tolerability on a five item questionnaire.

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EFFICACY AND TOLERABILITY OF ESIFAL• IN THE PROPHYLAXIS AND TREATMENT OF RADIATION-INDUCED ESOPHAGITIS IN PATIENTS WITH LOCOREGIONALLY ADVANCED BREAST CANCER (LABC)

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Aims: Adjuvant radiotherapy (RT) in LABC include the irradiation of breast or chest wall and regional lymphnode. Due to anatomical proximity of esophagus to supraclavicular lymphnodes, RT-induced esophagitis could be a frequent acute toxicity, presenting with throat pain, dysphagia and decreasing quality of life. Different studies report a benefit of mucosal protectors for the treatment of RT-induced esophagitis. Esifal® (Aurora Biofarma srl) is an oral supplement containing liquorice, greater plantain, hyaluronan, keratin and magnesium alginate and often given as mucosal protector. The aim of our study was to evaluate its tolerability and efficacy for prophylaxis and treatment of RT-induced esophagitis.

Method: From June 2021 to June 2022, 23 patients (pt) underwent adjuvant RT to breast or chest wall and regional lymphnode for LABC. RT was delivered using VMAT technique. The total dose prescribed was 48-50 Gy in conventional fractionation; in just one case hypofractionation regimen was chosen. Esifal was given at the beginning of RT and in 17 pt at the onset of esophagitis; it was prescribed twice a day, 30 minutes before meal. All pt were evaluated by a radiation oncologist at baseline, weekly and at the end of RT; acute toxicity was recorded according to CTACEvs5.

Result: All pt were female (100%) and the median age was 63 years (range 35-81). In 6 pt who received Esifal as prophylaxis, 4 (66.7%) had a complete benefit during the whole RT and concluded it without necessity of any other therapy. One pt had partial benefit for 14 days and one had no benefit, so other supportive care was prescribed. In the group where Esifal was given at symptoms, the median onset of esophagitis was at 20 Gy (range 14-28). A clinical benefit was recording in 11 cases (64,7%) and in 9 of these was kept till the end of RT. In 35,3% of pt there wasn't a benefit of Esifal, so different mucosal protectors or steroid have been started. Esifal was well tolerated in all the cohort. At the end of RT the main toxicity was G1; G2 esophagitis was reported in just one case. There was no G3 or higher toxicity or RT treatment interruption.

Conclusions: Based on our results we suggest the use of Esifal as a mucosal protector during regional nodal RT for LABC. Our data showed excellent tolerance and good response rate in both preventing and treating RT induced esophagitis in this subset of patients. A larger cohort study is needed to confirm our results, especially for prophylaxis use.

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PALLIATIVE RADIOTHERAPY FOR PAINFUL UNCOMPLICATED BONE MESTASTASES FROM HEPATOCELLULAR CARCINOMA

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Aims: The incidence of bone metastases(BM) in patients(pts) with hepatocellular carcinoma(HCC) has historically been low compared with those of other cancers, but has recently increased as a result of novel imaging techniques and prolonged survival of pts due to multidisciplinary treatment approaches.They are the most common source of moderate and severe cancer pain and can cause neurological symptoms that are detrimental to quality of life. Radiotherapy(RT) has not been frequently used in management of BM from HCC as evidenced by a limited number of retrospective reports. Purpose of the study was to evaluate the palliative effect of RT for painful uncomplicated BM from HCC.

Methods: From January 2009 to June 2022, 23 pts(F:3;M:20) with painful BM from HCC(56 sites, sts) were treated with external beam RT. Their ages ranged from 50 to 86 yrs(mean, 70 yrs).Among them, there were 11 pts(69,5%) with metastases to other organs, 8 pts(34.7%) had a solitary BM and 15 pts(65.2%) had multiple BM. Radiation volume involved gross tumor volume established by CT scan. Pts were treated using 3D-conformal RT or VMAT. The total dose of RT ranged from 8 to 39 Gy(mean 20.4 Gy). Assessment of pain was on a Numerical Rating Scale(NRS) from 0 to 10, with value of 0 as no pain and 10 as maximal pain.Responses for each irradiated st were evaluated 1 month(mt) after RT.

Results: 10 pts(19 sts) received an 8-Gy single fraction(SF), among them 4 pts received instead multiple fractions(MF), 1 at moderate doses(md) and MF at high doses(hd) (1 pt 20 Gy/25-36Gy; 3 sts) and MF at hd(3 pts 30-36 Gy; 7 sts). 19 pts(37 sts) received MF at md and hd, among them 7 received MF at md(15-20 Gy; 12 sts, including 1 pt that received also an 8-Gy SF and MF hd 25-36 Gy; 3 sts), 12 pts received and MF at hd(25-39 Gy; 23 sts), including 4 pts that received also an 8-Gy SF(6 sts) and 1 pt received instead a md fractions 20 Gy(1 st) and 1 pt that received also 20 Gy MF(5 sts). The most frequent st was the vertebrae(58,9%). Pain relief was obtained for 91,3%(21/23) of BM. Treatments were well tolerated. SF was as effective as MF RT in terms of pain relief. Of the sts in which response was achieved, the response duration was significantly longer for the MF group than the SF group(1.9 mts vs 8.4 mts, respectively; p = 0.004).Median survival time from the start of RT was 6.68 mts.

Conclusion: RT provides effective palliation for pts with painful BM from HCC during the substantial median survival time.

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WHY IS PAIN POORLY MANAGED IN BREAST CANCER PATIENTS? A MULTICENTER ANALISIS ON 2104 PATIENTS FROM 13 ITALIAN RADIOTHERAPY DEPARTMENTS

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Aim: Treatment of pain is frequently inadequate in cancer patients, especially in subjects with non-neoplastic pain (versus neoplastic) and undergoing curative treatment (versus palliative). Moreover, several studies based on the Pain Management Index (PMI) showed that also breast cancer (BCa) is correlated with pain under-treatment. Aim of this analysis is to evaluate whether the poor pain management in BCa patients is due to the non-neoplastic origin of pain (from surgical scar) and to the adjuvant purpose of therapy in most subjects and/or to the female gender.

Methods: Data on gender, age, ECOG Performance Status, RT aim, primary tumor, tumor stage, intensity of pain measured with the Numeric Rating Scale (NRS), type of pain (cancer pain [CP], non-cancer pain [NCP], mixed pain [MP]) were collected. A Pain Score was defined with values between 0 (no pain; NRS: 0) and 3 (severe pain; NRS: 7-10). An Analgesic Score was defined with values between 0 (no pain medication) and 3 (use of strong opioids). The PMI was calculated by subtracting the pain score from the analgesic score. A negative PMI value indicates an inadequate analgesic prescription. This study was approved by the Ethical Committee of the participating centers (ARISE-1 study).

Table 1. Comparison between breast cancer and other tumor in terms of inadequate pain management (PMI < 0). Only 1417 patients with pain or under analgesic therapy were included.

All treatments		PMI < 0 all patients			PMI < 0 cancer pain			PMI < 0 non-cancer pain			PMI < 0 mixed pain	
	n	n	%	N	n	%	n	n	%	n	n	%
breast	435	263	60.5	161	62	38.5	217	176	81.1	57	25	43.9
others	982	376	38.3	540	152	28.1	239	150	62.8	203	74	36.5
p-value		0.000			0.012			0.000			0.309	
	n	n	%	N	n	%	n	n	%	n	n	%
breast	435	263	60.5	161	62	38.5	217	176	81.1	57	25	43.9
endometrium/cervix	79	39	27.3	33	10	30.3	37	26	70.3	9	3	33.3
p-value		0.065			0.374			0.131			0.553	
Palliative	n	n	%	N	n	%	n	n	%	n	n	%
breast	175	55	31.5	131	42	32.0	5	3	60.0	39	10	25.6
others	562	163	29.0	401	104	26.0	35	22	62.8	126	37	29.3
p-value		0.539			0.173			0.902			0.653	
Curative	n	n	%	N	n	%	n	n	%	n	n	%
breast	260	208	80.0	30	20	66.6	212	173	81.6	18	15	83.3
others	420	213	50.7	139	48	34.5	204	128	62.7	77	37	48.0
p-value		0.000			0.001			0.000			0.007	

Results: The results of our study are shown in Table 1. The analysis confirmed the lower adequacy of pain management in BCa patients, with statistically significant differences in both subjects with CP and NCP. However, the incidence of PMI<0 was significantly higher only in BCa patients undergoing curative therapy and not in those treated with palliative radiotherapy. Finally, the incidence of PMI<0 was more than double, in patients with BCa, compared to patients with other female cancers (cervix, endometrium) with a trend towards statistical significance.

Conclusions: Inadequate pain management in BCa is largely, but not only, due to the curative intent of therapy in the majority of patients and particularly to the very high rate (81.1%) of patients with PMI<0 within subjects with NCP. Instead, belonging to the female gender does not represent in itself a cause of inadequate pain management.

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A FRAMEWORK OF THE PALLIATIVE TREATMENTS AND POSSIBLE ROLE OF PROGNOSTIC SCORE IN 2021 CLINICAL ACTIVITY: MONOCENTRIC EXPERIENCE

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Aims: Palliative radiotherapy (RT) plays an important role in patients with metastatic disease (MD) for symptom and local control, as well as patients' quality of life. A variety of indications and RT prescriptions exists. In the age of oligometastatic disease (OD) and potential curability through combined systemic and local ablative therapies such as stereotactic radiotherapy (SRT) we report a framework of palliative treatments in our RT department and the application of two prognostic models to investigate their potential role in daily practice.

Methods: We retrospectively reviewed all patients treated from 1/1-31/12/2021. OD was defined as the presence of 3-5 metastases while plurimetastatic disease implied increased tumor burden. Two prognostic scores were used. The Chow score (CS) involves 3 variables (non breast cancer, metastases other than bone, and Karnofsky performance status (KPS)≤ 60), defining 3 groups: poor prognosis when all conditions were present (score 3), intermediate prognosis when 2 conditions were present (score 2) and good prognosis when 0-1 conditions were present (score 1). The Oswestry Risk Index (ORI) focuses on rate of growth of primary tumour (score 1-4) and KPS (score 0-2) Table 1.

Results: Two hundred and ten patients received a treatment for MD:181with palliative intent (86%) and 29 for stereotactic ablative intent (14%). Oligometastatic patients were submitted to SRT for bone, lung and brain lesions. The median age was 65,5 years (22-94) while a moderate KPS was registered in 61% of patients. Cumulative percentage of prostate and breast cancer patients was 47%. The median CS value was 1,6 (0-3)

while median ORI was 2,8 (1-6). For palliative intent the main used RT schedule was single fraction and the most frequent site of irradiation was pelvic bone. Intensity Modulated Radio Therapy was delivered in 35 patients (19%). *Conclusions:*We provided the report of palliative spectrum in our RT daily activity. Median values of two prognostic scores used showed that in most of cases the indication of palliative RT is given in patients with a good-moderate expectancy of life and a good KPS. Since the difference between treatments with palliative intent and stereotactic radiotherapy (86% vs. 14%), multidisciplinarity in the oligometastatic setting is required to intercept these patients. The application of prognostic models could help in the selection of patients and therefore in the intensification of the RT dose in borderline cases.

Table 1.

Table 1 Clinical and treatment characteristics of palliative patients

KPS			Good 80-100%	67 (37%)
			Moderate 50-70%	110 (61%)
			Poor 10-40%	4 (2%)
Primary tumor			Type	n. patients. Tot 181
			Breast	67
			Prostate	18
			Gastrointestinal	15
			Others	81
Fractionation schedule			800 cGy	75
			2000 cGy (400 cGy per fraction)	97
			3000 cGy (300 cGy per fraction)	9
INTENSITY MODULATED RADIOTHERAPY				35
SITE OF RADIOTHERAPY			WHOLE BRAIN	17
			LUMBAR SPINE	23
			DORSAL SPINE	40
			CERVICAL SPINE	9
			PELVIC BONE	43
			OTHERS	47
Prognostic Scores	Chow score	Primary cancer	Breast=0	67
			Other =1	114
		Site of metastases	Bone only=0	62
			Other =1	119
		KPS	>60	117
			≤60	64
		SUM POINTS	0-1 (35-64 months)	83
			2 (19-28 months)	65
			3 (9-10 months)	33
	OSWESTRY RISK INDEX	Primary tumor pathology	Slow growth: breast, thyroid, prostate, myeloma, hemangioma, endothelioma, non-Hodgkin's lymphoma =1	86
			Moderate growth: kidney, uterus, tonsils, epipharynx, synovial cell sarcoma, metastatic thymoma =2	29
			Rapid growth: stomach, colon, liver, melanoma, teratoma, sigmoid colon, pancreas, rectum, unknown origin =3	21
			Very rapid growth: lung =4	44
		KPS	Good: KPS 80–100% =0	67
			Moderate: KPS 50–70% =1	110
			Poor: KPS 10–40% =2	4
		Sum points	1 (23 MONTHS)	33
			2-3 (6 MONTHS)	89
			4-5 (4 MONTHS)	58
			6 (2 MONTHS)	1
			7 (1 MONTH)	0

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SYMPTOMATIC PALLIATIVE TREATMENT IN PATIENT WITH AMYLOIDOSIS

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We report the case of a 77-year-old female patient who in 2018 for the onset of pain vertebral body performed a dorsal CT (computer tomography) scan showing vertebral collapse at the level of D5-D7 with sleeve of tissue that surrounds the vertebral bodies on which surgery is performed stabilization of the vertebrae and sampling of tissue for histological evaluation that finds immunohistochemical positivity to immunostaining for amyloid. In November 2021 due to worsening of painful symptoms she started therapy with oxycodone 30 mg x 2.die and carried out radiological investigations with MRI (magnetic resonance imaging) of the spine showing persistence of large signal tissue inhomogeneous and impregnated with contrast agent at the level of the stretch D7-D9, extended on site paravertebral and in the anterior area where imprinted the aorta. The fabric extended inside the anterior portion of the vetebral canal in the epidural and impressed the medulla. Extension longitudinal of about 5 cm and transverse diameter of about 2 cm, in the paravertebral area rear left. In December she reports onset of walking disorders. Proposed surgical intervention patiente refused, preferring the radiotherapic option. In January 2022 the patient was therefore subjected to radiotherapy with the 3d technique for one total dose of 36 Gy in 20 fractions of 1.8 Gy each at the level of D7-D9. After 3 months from the end of the treatment, the patient no longer reports any pain relief or neurology. She has also stopped taking pain relief therapy

Results: After 3 months from the end of the treatment, the patient no longer reports any pain relief or neurology. She has also stopped taking pain relief therapy

Conclusions: Radiotherapic treatment for palliative purposes in patients with vertebral amyloidosiscan be considered effective and minimally invasive.

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PATTERN OF CARE FOR THE USE OF SRT IN OLIGOMETASTATIC PATIENTS: THE CAMPANIA OLIGO-RT PROJECT

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Aims: Recently, the definition of oligometastatic disease has greatly changed the cancer landscape, highlighting the opportunity of reaching a prolonged control of disease or even a cure for a subset of metastatic patients, with either radiotherapy (RT) or surgery. The AIRO Campania Regional society has performed a retrospective evaluation of patients that underwent stereotactic RT (SRT) in this setting, to understand the critical issues and to spread the knowledge of this approach.

Method: Clinical and technical radiotherapy parameters of oligometastatic patients undergoing SRT from January 2019 to April 2022. Toxicity, follow up, regional control, distant metastasis and overall survival have also been analyzed.

Results: 326 patients from 8 different centers have been included in the present analysis (205 males and 121 females). Most of the patients were referred for RT from the Medical Oncologist (190 patients, 58,3%), other were referred from multidisciplinary tumor board (MTB: 90 patients, 27,6%) or from other Specialists (46 patients, 14,1%). SRT was directed to brain (140 patients, 42,9%), lung (69 patients, 21,2%), bone (42 patients, 12,9%), nodes (67 patients, 20,6%), liver (2 patients, 0,6%) or other districts (6 patients, 1,8%). Most of the patients were under systemic therapy during SRT (216 patients, 66,3%) and median prescription dose was 27 Gy (mean 29 +/- 10,4 Gy), with a median number of 5 fractions (mean 5 +/- 1,2, range 1-8 fx). Acute and subacute toxicity due to SRT was scaled as G0 in 242 patients (74,2%), G1 in 71 patients (21,8%), G2 in 11 patients (3,4%) and G3 in 2 patients (0,6%). At the first restaging after SRT, 39 patients (11,9%) showed a complete response, 66 patients showed a partial response (20,2%), 107 patients showed a stability of disease (32,8%), 39 patients showed a progression of disease (11,9%) and 66 patients were lost at follow up (20,2%). Only a limited percentage of patients were available for a follow up > 6 months after SRT (56 patients, 16,9%), with a mean OS of 45 +/- 3,6 months (median not reached).

Conclusions: The project confirms that SRT is increasingly used for oligometastatic patients, with good profile of safety and efficacy. Conversely, better communication is needed in the MTB to propose this strategy to a high number of patients. Lastly, follow up of radiotherapy patients is pivotal to better understand the late toxicity profile and to propose salvage strategies at the disease recurrence.

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PATTERN OF DISEASE PROGRESSION FOLLOWING LOCOREGIONAL TREATMENT IN OLIGOMETASTATIC STS PATIENTS

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Aims: Locoregional treatments (LT) for oligometastatic soft tissue sarcoma (STS) are increasingly used, especially in light of the poor response to chemotherapy. However, the impact of LT on disease control is debated, in particular due to risk of early polymetastatic conversion. In this study we retrospectively analyzed the clinical course of oligometastatic STS after LTs.

Methods: In this retrospective and monocentric study we evaluated a cohort of patients with oligometastatic (i.e. 5 extracranial metastasis) STS, treated with SBRT and/or surgical treatment from February 2014 to April 2022. For each patient clinical data, age, sex, STS site, chemotherapy prior to LT, LT type (surgery/SBRT), number of LT and the interval from first diagnosis to metastatic relapse (cut-off: 24 months) were recorded. Disease free survival (DFS), wide spread progression (WSP, corresponding to multiple site progression no longer treatable with locoregional strategies), and overall survival (OS) were calculated from date of LT to event, last follow-up visit or death. Statistical analysis was performed with MedCalc v. 1.8 to identify predictors of improved outcome.

Results: Nineteen oligometastatic STS patients were included in our study. Median age was 50 years (range: 39-72): primary site was located in the limbs in 68% of patients. Adjuvant chemotherapy was administered in 70% of patients. Oligometastatic disease occurred within 24 months from diagnosis in 8 patients (42%). All patients were treated with LT; 35% (n=6) received only surgery, 15% (n=4)only SBRT and 50% (n=9) received both. The median number of LT per patient was 2 (range: 1-6). Median DFS, WSP and OS were respectively 12 months (95% CI 3-19), 28 months (95% CI 22-53) and 35

months (95% CI 26-35). At the univariate analysis no significant differences in DFS and OS were found, according to age, sex, histology, site of STS, adjuvant chemotherapy, number of LT and interval from diagnosis to metastatic relapse. A longer delay to WSP was observed in patients who experienced first metastatic recurrence 24 months from diagnosis (median 9 vs 53 months, p= 0.031, HR 0.30 0.05-1.6).

Conclusions: Oligometastatic STS patients treated with LT experience a long progression-free interval and promising OS. Polymetastatic conversion is a late event, in particular in patients with a long interval from primary diagnosis to first metastatic relapse. Repeated LTs may be administered to extend disease control.

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THE ROLE OF SBRT FOR THE TREATMENT OF ISOLATED LOCAL RECURRENCE OF RADICALLY RESECTED PANCREATIC CANCER

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Aims: Pancreatic adenocarcinoma is characterized by a poor prognosis, with a 5-years overall survival (OS) rate of only 6%. Even radically resected patients will develop disease recurrence within 2 years from surgery in a proportion variable from 60% to 80%, and 17-30% of patients will develop an isolated local recurrence. As these local recurrences are usually not resectable, the use of Stereotactic Body Radiation Therapy (SBRT) has emerged as a viable option. The aim of our study was to evaluate efficacy and feasibility of SBRT for selected patients with isolated local recurrence of pancreatic cancer after radical surgery.

Method: Patients treated with SBRT for isolated local pancreatic recurrence were retrospectively reviewed in this analysis. All patients were judged unresectable by multidisciplinar tumor board. Prescription dose was 45 Gy in 6 daily fractions. Primary end-point was Local Control (LC). Secondary end-points were Distant Progression-free Survival (DPFS), OS and toxicity.

Results: From February 2013 to March 2021, thirty-five patients with isolated local recurrence of radically resected pancreatic adenocarcinoma were treated at our institution with SBRT. Median LC was 30.2 months. Rates of LC at 1, 2 and 3 years were 67.8% (95%CI 47.9 – 81.4), 62.9% (95%CI 42.2 – 77.9), and 46.6% (95%CI 22.4 – 67.7) respectively. Median DPFS was 9.82 months. Rates of DPFS at 1,2 and 3 years were 44.0% (95%CI 26.9 – 59.9), 29.3% (95%CI 13.5 – 47.2) and 29.3% (95%CI 13.5 – 47.2) respectively. OS rates at 1, 2 and 3 years were 67.6% (95%CI 49.1 – 80.6%), 29.9% (95%CI 15.3 – 46.0), and 19.4% (95%CI 7.7 – 35.0) respectively. No cases of acute G3 or more toxicity occurred.

Conclusions: SBRT has proven to be an effective and safe option for isolated local recurrence of pancreatic cancer after radical surgery. Given the good local control rate, the very low toxicity profile, and the effective pain relief, the role of SBRT in these long-survivors selected patients is crucial in the multimodal approach to ultimately improve their survival and quality of life.

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INNOVATIVE REAL TIME TUMOR TRACKING ON HELICAL TOMOTHERAPY FOR SINGLE FRACTION SABR IN LUNG OLIGOMETASTASES: LATE EFFECTS AND EFFECTIVENESS

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Aims: Herein we report preliminary results of a small cohort of single fraction SABR, in patients with single and multiple lung oligometastases. This study investigates the feasibility, the compliance and preliminary late lung toxicity.

Materials: Lung tumor tracking allows to reduce the healthy tissue irradiation and is theoretically faster than the gating technique. Single fraction SABR in lung nodules is established as an appropriate treatment in oligometastatic patients. However, the risk of target missing in single fraction is higher than in fractionated SABR. Recently and only present in few centers worldwide, Accuray Int, developed a free breathing real time tumor tracking based on artificial intelligence for helical IMRT delivery (Synchrony on Radixact system). 28 Gy single fraction SABR (SFS) was planned in 13 patients in both peripheric and central lesions. In room time, nodule volumes, local response, real time tracking verification have been assessed for all the patients involved.

Results: Mean patients age was 77 years old (45-87) and 8 ones were men and the remaining 5 were women; in all cases their PS was 0-1. All patients had oligometastatic disease: primary melanoma (5), primary NSCLC (2) and CRC (1), HCC (1) and sarcoma (1). Concurrent immunotherapy (respectively Pembrolizumab, Nivolumab and Ipilimumab) was delivered in 8 patients. Lesions were both central (5/10) that peripheral (5/10). Mean GTV volume was 8,50 cc (from 1,9 cc up to 18,2 cc), minimum diameter of lesions was 129 mm to 312 mm. Median beam on time was 17,6 min (910 sec – 1255 sec). The analysis of the cumulative vector of nodules movement, measured a median excursion of 7 mm with a median respiratory cycle time of 4 seconds. No lesions progressed, due to the short follow up, the shrinkage

time-volume plot is currently under evaluation. Median follow-up was 8.5 months, during which we observed no clinical acute toxicity, four patients showed a radiological pattern of diffuse consolidation. All the lesions reduced their volume from 40% up to 90% within the first three months. For those patients with a follow-up longer than 1 year, the enlarged diffuse consolidation was reduced after 10 months after SABR.

Conclusions: The preliminary results of this cohort study, showed that lung SFS with Synchrony on Radixact system is a high compliance treatment in agnostic oligometastatic patients. This advanced technique needs a high expertise of all the personnel but is very promising.

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ROBOTIC STEREOTACTIC BODY RADIOTHERAPY (RSBRT) FOR OLIGOMETASTATIC AND OLIGOPROGRESSIVE ENDOMETRIAL CANCERS

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Aims: Endometrial cancer is the first gynecological malignancy for incidence, above all in most developed countries. The use of stereotactic body radiotherapy (SBRT) in the treatment of recurrent or metastatic endometrial cancer is a relatively new concept, with paucity of solid data in literature. This retrospective, monocentric study analyzed the efficacy and safety of robotic stereotactic body radiotherapy (rSBRT) in a cohort of patients with oligometastatic/oligoprogressive endometrial cancer.

Methods: We retrospectively analyzed data of women with endometrial cancer who underwent rSBRT treatments with CK technique between April 2013 and December 2021. For each SBRT treatment site, gross tumor volume (GTV), planning tumor volume (PTV), treatment prescription dose and fractions were recorded. Radiation biologically effective dose (BED), with an estimated α/β ratio of 10 was also calculated. Clinical outcomes in terms of local control (LC), 1 and 2-years-overall survival from rSBRT (yOSrSBRT) and adverse events were analyzed. Acute and late toxicities were assessed according to Common Terminology Criteria for Adverse Events (CTCAE) v. 5.0.

Results: Thirtysix patients' were treated on 52 metastatic lesions. Endometrioid endometrial cancer was the most common histotype (53%). Twentyfour patients (67%) received adjuvant radiotherapy previously, and 8 of them had infield rSBRT. Of the sites of metastatic disease, lymph node metastases were most common (50%) followed by bone (21%) and parenchima lesions (17%), with a median of one treatment for patient (range 1-3). The median dose and number of fractions were respectively 3000 cGy (range 1500-5600) and five (range 1-8). The median GTV and PTV volumes were respectively 14.22 cc (range 0.17-253,12) and 34.29 cc (range 0.22-332.79) while the median BED10 was 48 (range 37.5-100). LC was obtained in 73% of patients after rSBRT. The 1yOSrSBRT in patients who had local control vs patients who had not was respectively 90% and 40%, while the 2yOSrSBRT for the same groups of patients were 83% and 0% respectively. There was no grade >1 acute and late toxicity recorded.

Conclusions: Our retrospective analysis confirmed the efficacy of rSBRT and may be considered an effective safe option in oligoprogressive/oligometastatic endometrial cancer. Prospective studies are needed to further assess the use of rSBRT in this setting of patients.

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LIVER DEFORMABILITY AS RESIDUAL ERROR IN STEREOTACTIC RADIOTHERAPY OF HEPATIC METASTASES

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Aims: Breath control methods and image-guided radiotherapy (IGRT) are recommended techniques to online correct liver stereotactic radiotherapy (SRT) uncertainties. Liver deformability, that is a liver feature mainly influenced by neighboring OARs filling and position, represents an important issue in the setting of liver SRT, since it is not online correctable by IGRT. Aim of this study was to assess and offline quantify liver deformability as residual error after online IGRT match in patients treated with liver SRT in our Department.

Methods: The CBCTs from a sample of 8 patients with liver metastases were analyzed. CT simulation was performed with free breathing and with a specific technique for liver SRT: abdominal compression for 1 patient and breath hold for 7 patients. The radiotherapy treatment was provided through 3 or 5 fractions. Liver silhouette was offline delineated on each daily CBCT and compared to liver contour on planning CT. On the basis of liver/liver match between CT planning and each daily CBCT, liver center of mass shift on 3 axes (x, y and z) was evaluated. Dice Similarity Coefficient (DSC), as deformability index, was estimated.

Results: Breath hold technique was tolerated and reproduced. Liver deformability was evaluated for all the sample. The deviation standard for the center of mass shift was evaluated for the 3 axes in all the patients, as shown in Table 1. According to the results, the liver

deformability is bigger in the – X axe, probably due to the interfraction filling variation of the abdominal hollow organs (stomach, bowel). This was considered as a preliminary result of interfraction Internal Margin (IM) to extend PTV margin. A limit of the study was the possible presence of artifacts in the CBCT images that can make less accurate the liver contouring. The mean DSC was 0.87.

Conclusion: Our results demonstrated that, although breath hold technique resulted an effective technique for liver SRT, with a residual organ motion < 5 mm, liver deformability represented a residual error that is not online correctable, to consider also in breath hold patients. Deformability was offline quantified for all patients and considered as IM for the PTV definition, with an additional margin of 2 mm. We analyzed the whole liver: it will be interesting to evaluate the partial deformability of the liver, related to the position of the lesion.

Table 1. Mean liver deformability standard deviation.

	Motion Management	Center of Mass shift - X (cm) [lateral]	Center of Mass shift - Y (cm) [longitudinal]	Center of Mass shift - Z (cm) [anterior posterior]
Patient 1	Abdominal Compression	0,31	0,16	0,21
Patient 2	Breath Hold	0,76	0,12	0,26
Patient 3	Breath Hold	0,28	0,27	0,49
Patient 4	Breath Hold	0,23	0,22	0,26
Patient 5	Breath Hold	0,16	0,18	0,31
Patient 6	Breath Hold	0,23	0,32	0,15
Patient 7	Breath Hold	0,33	0,39	0,46
Patient 8	Breath Hold	0,59	0,48	0,45
Standard Deviation		0,21	0,13	0,13

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COMPARISON OF TWO DIFFERENT TECHNIQUES IN ROBOTIC STEREOTACTIC BODY RADIOTHERAPY IN PROSTATE CANCER PATIENTS: AN INITIAL MONOINSTITUTIONAL EXPERIENCE

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Aim: Stereotactic body radiotherapy (SBRT) is a treatment option in prostate cancer (PCa) patients (pts), with clinical and toxicity outcomes comparable to standard fractionation. The aim of this retrospective monoinstitutional analysis is to compare two different techniques of prostate robotic SBRT (CyberKnife, Accuray, Sunnyvale, CA, USA): homogeneous versus urethral sparing HDR-like dose distribution.

Methods: Between 10/2017-04/2022, 128 patients with PCa were treated using a robotic SBRT. Pts characteristics are reported in Table 1. Four fiducial markers were implanted into the prostate in all pts. In 40 pts neoadjuvant hormonal therapy was prescribed in order to reduce the prostate volume and, theoretically, radiotherapy toxicity. Furthermore, in 93 pts steroid therapy and/or alpha-lytics were prescribed, at the beginning of the radiation treatment, to prevent side effects. Two different techniques were used. The first one (H, in 76 pts) aimed to achieve a dose into the prostate gland as homogeneous as possible, with a prescription dose of 36.25 Gy in 5 fractions, corresponding to EQD2 91 Gy (using the classic α/β 1.5) or 67 Gy (using the α/β 4.2 recently proposed by Cui for SBRT). The other technique (US, in 52 pts) tried to mimic HDR brachytherapy, creating a minor dose area around the urethra, identified by the placement of a catheter; in this group the dose prescription was 38 Gy in 4 fractions (114 Gy with α/β 1.5 or 81 Gy with α/β 4.2), with the following urethral constraints: maximum dose: 45.6Gy; D50<39.9 Gy and D10<41.8 Gy. Toxicity was scored in accordance with CTCAE v 5.0. Biochemical failure was assessed using the nadir + 2 definition.

Results: Median follow-up was 27 (1-53) months. At the last follow up 7 pts died due to a non-cancer related cause, 3 pts had a biochemical failure with PSMA/Choline-PET indicating disease progression: 2 of the H group and 1of the US group. Biochemical RFS, OS and DFS are not significantly different between the two groups. The treatment was well tolerated with no G3 acute events. In the H group, 7 G3 late event are reported, while in US group only one rectal toxicity was assessed (p-value=0.3).

Conclusion: Despite a short and not comparable follow up between the two groups, US technique seems to allow dose escalation without increasing G3 toxicity. Longer follow-up is needed to confirm these result and to try to find an advantage of dose escalation on clinical outcomes.

Table 1.

	H group	US group
Number of patients	76	52
Median age (range)	74.9 (55.8-85.3)	75.2 (48.8-83.9)
Initial PSA (range)	7.2 (2.17-9.67)	7.72 (2.43-27)
Risk group		
-low risk	8 (10.5%)	6 (11.6%)
-intermediate risk	65 (85.5%)	43 (82.7%)
-high risk	2 (2.7%)	2 (3.8%)
-oligometastatic	1 (1.3%)	1 (1.9%)
Gleason score		
-3+3	18 (23.7%)	12 (23.1%)
-3+4	44 (57.9%)	28 (53.8%)
-4+3	13 (17.1%)	11 (21.2%)
-4+4	0	1 (1.9%)
-NA	1 (1.3%)	0
ADT		
-yes	29 (38.2%)	11 (21.2%)
-no	47 (61.8%)	41 (78.8%)
Median follow up, months	30.7 (2-53)	12.7 (1-49.2)

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STEREOTACTIC BODY RADIATION THERAPY FOR LIVER METASTASES IN OLIGOMETASTATIC PATIENTS AND IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Aims: To evaluate feasibility and efficacy of Stereotactic Body Radiation Therapy (SBRT) for unresectable liver metastases in oligometastatic patients (pts) and in pts with hepatocellular carcinoma (HCC).

Method: Between June 2021 and May 2022 we treated 16 pts with SBRT to the liver: 6 were female and 10 were male. Median age was 74.5 years (range 56-90 years). Number of lesions per patient varied between 1 and 3. Eight pts had a diagnosis of HCC and eight were oligometastatic patients (one breast cancer, one lung cancer, six gastrointestinal cancer). Radiotherapy prescription dose ranged from 27 Gy to 50 Gy (median 50 Gy) in 3-7 fractions (median 5 fractions). Patients were simulated using an abdominal compression device and a 3-phase contrast-enhanced CT scan. For the treatment a volumetric modulated arc therapy (VMAT) technique was used, while for image guidance a Cone beam CT (CBCT) was used before each fraction with online correction.

Results: There were no adverse effects. Treatment was well tolerated: according to NCI CTCAE v5.0 hepatobiliary toxicity scale, no acute toxicity > G0 was recorded. Of the eleven pts that have already been re-staged with MRI or CT, five were in complete response, three in partial response and 3 had a stable disease.

Conclusions: Stereotactic body radiation therapy is a non-invasive, well-tolerated and effective treatment for patients with HCC or liver metastases not suitable for surgical resection or for other local treatments.

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1-WEEK HYPOFRACTIONATED ADJUVANT WHOLE-BREAST RADIOTHERAPY: UPDATE OF INSTITUTIONAL CASE SERIES AND LITERATURE REVIEW

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Aims: Our preliminary clinical experience on 7 early breast cancer (EBC) patients confirmed published data on feasibility, good early tolerance and effectiveness of adjuvant breast radiotherapy (RT) with 1-week hypofractionated regimen. Here, we report an update of our institutional case series and a literature review to support this practical approach for selected EBC cases (e.g., elderly women with concomitant conditions limiting the adherence to prolonged fractionation schedules).

Methods: From December 2020 to May 2022, 20 early breast cancer (EBC) patients (age ≥ 79 years and/or affected by comorbidities) were treated at our Radiation Oncology Unit with 1-week hypofractionated adjuvant whole-breast RT. The whole breast was contoured as CTV. A total dose of 26 Gy (FAST-Forward protocol) or 27 Gy in 5 daily fractions was prescribed to the PTV. RTOG skin toxicity was evaluated during treatment and follow up period. We also performed a Pubmed-PICO search with the following keywords: P (breast cancer) I (Short course hypofractionated whole breast irradiation) – C/O (not explored).

Results: Among our patients, right breast was irradiated for 10 cases, while a bilateral breast irradiation was performed for a 84-years old patient. All treatments were delivered with VMAT technique and daily IGRT with Surface-Guided Radiotherapy with no tatoo references. Satisfactory target coverage and respect of OARs contraints (Heart: V1.5<30%, V7<5%; omolateral lung: V8<15%) were obtained in all plans. No RT-related cutaneous toxicity (RTOG score 0) was observed during treatment. Mean follow up was 11 months. RTOG grade 2 skin oedema was reported for two patients; instrumental and clinical examination confirm a complete tumor local control. Among 11 studies indentified through a Pubmed-PICO search, only 4 papers (3 reviews and 1 clinical study after lumpectomy) reported on 1-week hypofractionated regimen in EBC.

Conclusions: Our clinical experience on a larger sample size with prolonged follow up and recent published data support the use of five-fractions schedule within one week in selected EBC cases, due to its good tolerance and effectiveness. Cost-effectiveness could be improved due to better treatment completion rates, optimal tumor control rate in elderly patients (with limited treatment compliance for comorbidities, pandemic emergency, etc.), as well as no significative incidence of severe toxicities requiring treatments.

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COVID-19 AND RADIOTHERAPY: A SYSTEMATIC REVIEW AFTER 2 YEARS OF PANDEMIC

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Aims: Following the Covid-19 pandemic spread, changes in clinical practice were necessary in order to limit the pandemic diffusion. Also, oncological practice has undergone changes with radiotherapy (RT) treatments playing a key role. Although several experiences have been published, the aim of this review is to summarize the current evidence after 2 years of pandemic in order to provide useful conclusions for clinicians.

Methods: A Pubmed/MEDLINE and Embase systematic review was conducted. The search strategy was "Covid AND Radiotherapy" and only original articles in the English language were considered.

Results: A total of 2.733 papers were obtained using the mentioned search strategy. After the complete selection process, a total of 281 papers were considered eligible for the analysis of the results.

Conclusions: RT has played a key role in Covid-19 pandemic as it has proved more resilient than surgery and chemotherapy. The impact of the accelerated use of hypo fractionated RT and telemedicine will make these strategies central also in the post-pandemic period .

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PALLIATIVE TREATMENTS IN SARS COVID 19 PANDEMIC TIME

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Aims: To evaluate the load of palliative treatments in two radiation therapy units during Sars Covid 19 pandemic.

Methods: From January 2019 to December 2021 a total of 888 palliative treatments were performed in two radiotherapy centers.

Results: Of these 888 treatments, 535 were directed to bone metastasis, 308 were WBRT, 45 others (*i.e.* mediastinal syndrome, haemostatic treatments, etc). Different RT schemes were used, especially to treat bone metastasis. In particular a dose of 8 Gy/1 fx in 265 cases; 10 Gy/1 fx in 3 cases; 12 Gy/1fx in 1 case; 19.5-24 Gy/3fx in 8 cases; 20 Gy/4fx in 194 cases; 20 Gy/5 fx in 50 cases; 30 Gy/10 fx in 14 cases. We noticed a general increase in palliative treatments for bone metastasis during the pandemic period (200 in 2020 vs 168 and 167 in 2019 and 2021 respectively). These differences add a statistically significant value (p=0,0003). In addition, most used fractionation in 2020 was 8 Gy in single fraction. Precisely: 103 in 2020, 80 in 2019 and 81 in 2021.

Conclusions: The increased treatment's number observed in 2020 could be linked to a lesser systemic prescription during pandemic, reserving local therapy in a higher case with respect to non-pandemic time. Besides the greater use of single fraction in 2020 could be linked to the necessity to decrease hospital accesses during pandemic.

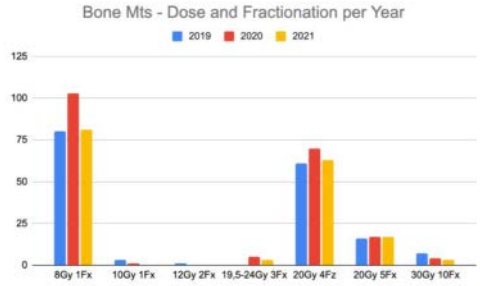

Figure 1.

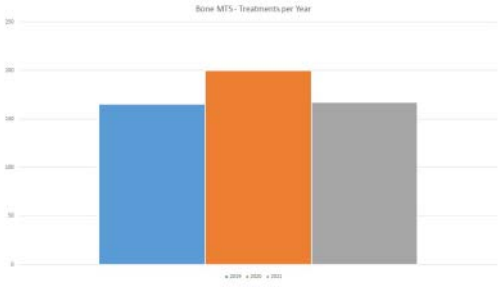

Figure 2.